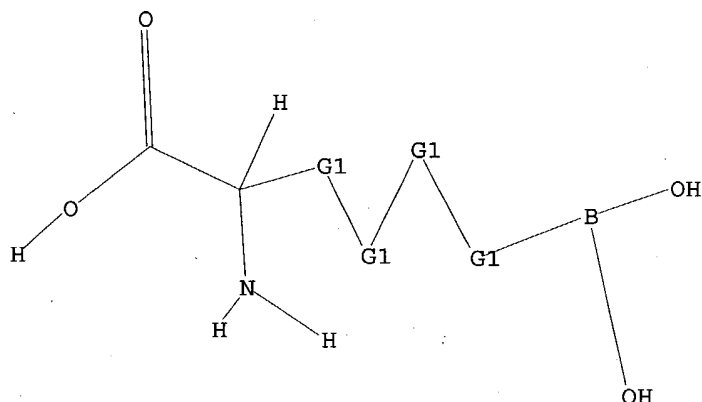


=> d  
 L1 HAS NO ANSWERS  
 L1 STR



G1 CH2,O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1  
 SAMPLE SEARCH INITIATED 12:20:43 FILE 'REGISTRY'  
 SAMPLE SCREEN SEARCH COMPLETED - 31 TO ITERATE

100.0% PROCESSED 31 ITERATIONS 0 ANSWERS  
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
 BATCH \*\*COMPLETE\*\*  
 PROJECTED ITERATIONS: 286 TO 954  
 PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full  
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 FULL SCREEN SEARCH COMPLETED - 460 TO ITERATE

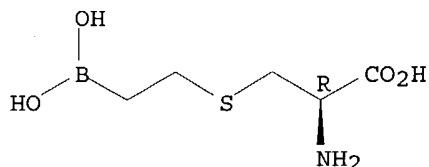
100.0% PROCESSED 460 ITERATIONS 5 ANSWERS  
 SEARCH TIME: 00.00.01

L3 5 SEA SSS FUL L1

=> d 1-5

L3 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 222638-67-7 REGISTRY  
 CN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C5 H12 B N O4 S . Cl H  
 SR CA  
 LC STN Files: CA, CAPLUS, CHEMCATS, USPAT2, USPATFULL  
 CRN (63107-40-4)

Absolute stereochemistry.

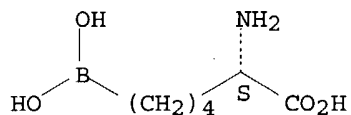


● HCl

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 222638-65-5 REGISTRY  
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C6 H14 B N O4  
CI COM  
SR CA  
LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

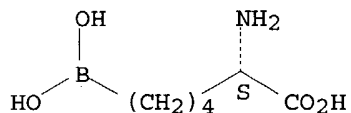


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

9 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 194656-75-2 REGISTRY  
CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C6 H14 B N O4 . Cl H  
SR CA  
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL  
CRN (222638-65-5)

Absolute stereochemistry.

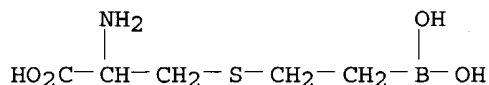


● HCl

3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN

RN 88642-86-8 REGISTRY  
 CN Alanine, 3-[(2-boronoethyl)thio]- (7CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN NSC 77838  
 MF C5 H12 B N O4 S  
 LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS  
 (\*File contains numerically searchable property data)

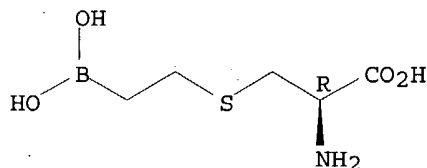


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 63107-40-4 REGISTRY  
 CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN S-(2-Boronoethyl)-L-cysteine  
 FS STEREOSEARCH  
 MF C5 H12 B N O4 S  
 CI COM  
 LC STN Files: BEILSTEIN\*, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

8 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	165.53	167.00

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FILE COVERS 1907 - 26 Apr 2004 VOL 140 ISS 18  
FILE LAST UPDATED: 25 Apr 2004 (20040425/ED)

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> s 13

L4 14 L3

=> d ibib abs hitstr 1-14

L4 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:757815 CAPLUS  
DOCUMENT NUMBER: 139:271048  
TITLE: Modulation of the immune response through the  
manipulation of arginine levels  
INVENTOR(S): Ochoa, Augusto C.; Ochoa, Juan B.; Popescu, Mircea;  
Zea, Arnold H.; Rodriguez, Paulo C.  
PATENT ASSIGNEE(S): LSU Medical Center, USA  
SOURCE: PCT Int. Appl., 127 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078578	A2	20030925	WO 2003-US7523	20030312
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2004057926 A1 20040325 US 2003-386131 20030312

PRIORITY APPLN. INFO.: US 2002-363366P P 20020312

AB The invention provides methods and compns. for modulating an immune response by controlling the level of arginase available to a cell, tissue or system. An immune response can be enhanced or depressed by altering the amount of arginine available to a cell, tissue or system through the manipulation of localized or systemic arginine levels using substances which provide arginine to the body and enzymes which break down arginine, e.g. arginase and nitric oxide synthase. Increasing or decreasing an immune response according to the invention provides therapeutic treatment for a variety of conditions and diseases. The invention also provides clin. methods and kits which can measure the strength or resistance to an immune response in a cell, tissue or system based upon the amount of available arginine and enzymes which break down arginine.

IT 63107-40-4 222638-65-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

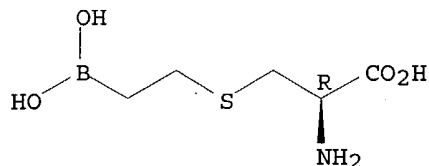
(Biological study); USES (Uses)

(arginine level manipulation for immune response modulation)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

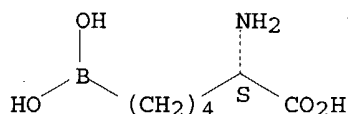
Absolute stereochemistry.



RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:485171 CAPLUS

DOCUMENT NUMBER: 139:175824

TITLE: Human Arginase II: Crystal Structure and Physiological Role in Male and Female Sexual Arousal

AUTHOR(S): Cama, Evis; Colleluori, Diana M.; Emig, Frances A.; Shin, Hyunshun; Kim, Soo Woong; Kim, Noel N.; Traish, Abdulmaged M.; Ash, David E.; Christianson, David W.

CORPORATE SOURCE: Roy and Diana Vagelos Laboratories Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA

SOURCE: Biochemistry (2003), 42(28), 8445-8451

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Arginase is a binuclear manganese metalloenzyme that catalyzes the hydrolysis of L-arginine to form L-ornithine and urea. The X-ray crystal structure of a fully active, truncated form of human arginase II complexed with a boronic acid transition state analog inhibitor has been determined at 2.7 Å resolution. This structure is consistent with the hydrolysis of L-arginine through a metal-activated hydroxide mechanism. Given that human arginase II appears to play a role in regulating L-arginine bioavailability to NO synthase in human penile corpus cavernosum smooth muscle, the inhibition of human arginase II is a potential new strategy for the treatment of erectile dysfunction. Since NO synthase is found in human clitoral corpus cavernosum and vagina, we hypothesized that human arginase II is similarly present in these tissues and functions to regulate L-arginine bioavailability to NO synthase. Accordingly, hemodynamic studies conducted with a boronic acid arginase inhibitor in vivo are summarized, suggesting that the extrahepatic arginase plays a role in both male and female sexual arousal. Therefore, arginase II is a potential target for the treatment of male and female sexual arousal disorders.

IT 63107-40-4D, L-Cysteine, S-(2-boronoethyl)-, complexes with arginase II

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL

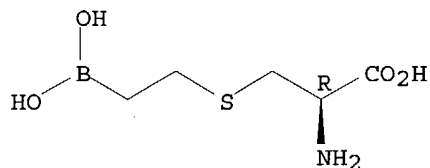
(Biological study)

(crystal structure of human arginase II complexed with boronic acid transition state analog inhibitor and physiol. role of arginase II in male and female sexual arousal)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



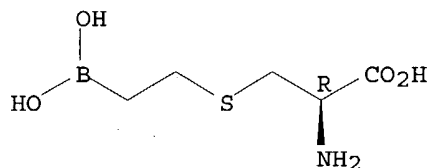
IT 63107-40-4 222638-65-5

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(crystal structure of human arginase II complexed with boronic acid transition state analog inhibitor and physiol. role of arginase II in male and female sexual arousal)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

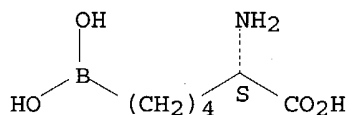
Absolute stereochemistry.



RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

37

THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:667433 CAPLUS

DOCUMENT NUMBER: 137:206548

TITLE: Herbal composition for inhibiting arginase and enhancing sexual response

INVENTOR(S): Heleen, Pamela A.

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 5 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6444237	B1	20020903	US 2001-952275	20010913

PRIORITY APPLN. INFO.: US 2001-952275 20010913

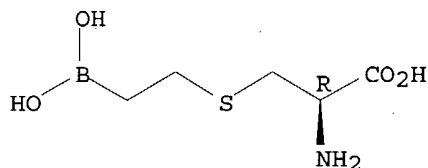
AB A unique combination of herbal ingredients designed to overcome natural inhibitors of human sexual response and allow for improved response and psychol. effects is described. The composition is comprised of exts. taken from Crataegus monogyna berry, Turnera diffusa, Pfaffia paniculata, Ginkgo biloba, Pygeum africanum, and ginsenosides extract, that are combined with L-arginine, L-glutamic acid and L-theanine in amts. effective to produce desired results. For example, a powder formulation contained L-arginine 1.5 g, L-glutamic acid 0.15 g, C. monogyna berry extract 0.08 g, T. diffusa extract 0.07 g, P. paniculata extract 0.07 g, G. biloba extract 0.06 g, P. africanum extract 0.05 g, L-theanine 0.04 g, and ginsenosides mixture 0.02 g. After oral administration (mixed with water), more pronounced sexual response was reported by a majority of participants in comparison to the com. product (Sexual Performance Enhancer).

IT **63107-40-4**, S-(2-Boronoethyl)-L-cysteine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (exts.; herbal comps. for inhibiting arginase and enhancing sexual response)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:367283 CAPLUS

DOCUMENT NUMBER: 136:355488

TITLE: Preparation of borono amino acids as arginase inhibitors

INVENTOR(S): Christianson, David; Baggio, Ricky; Elbaum, Daniel

PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA

SOURCE: U.S., 64 pp., Cont.-in-part of Appl. No.

PCT/US98/21430.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6387890	B1	20020514	US 2000-545737	20000410
WO 9919295	A1	19990422	WO 1998-US21430	19981009
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2003036529	A1	20030220	US 2002-53939	20020123
US 6723710	B2	20040420		
US 2004063666	A1	20040401	US 2003-661965	20030912
PRIORITY APPLN. INFO.:				
			US 1997-61607P	P 19971010
			WO 1998-US21430	A2 19981009

US 2000-545737 A3 20000410  
US 2002-53939 A1 20020123

OTHER SOURCE(S): MARPAT 136:355488

AB Borono amino acids HO<sub>2</sub>CCH(NH<sub>2</sub>)-X<sub>1</sub>-X<sub>2</sub>-X<sub>3</sub>-X<sub>4</sub>-B(OH)<sub>2</sub> (X<sub>1</sub>-X<sub>4</sub> = CH<sub>2</sub>, S, O, NH, N-alkyl) and compns. and methods for inhibiting arginase activity using borono amino acids are described. Thus, 2(S)-amino-6-boronoheptanoic acid, prepared in 5 steps from Boc-Glu-OCMe<sub>3</sub> via conversion to the side chain aldehyde, Wittig olefination with Ph<sub>3</sub>P:CH<sub>2</sub>, hydroboration with BH<sub>3</sub>, trapping with (1S,2S,4R,6S)-(+)-pinanediol, and deprotection with BCl<sub>3</sub>, inhibited arginase with K<sub>i</sub> = 0.1 μM.

IT 63107-40-4P 222638-65-5P 222638-67-7P

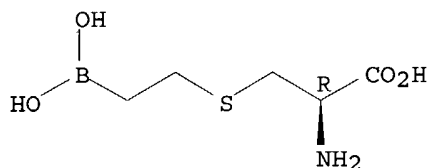
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of borono amino acids as arginase inhibitors)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

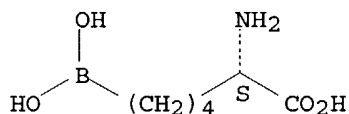
Absolute stereochemistry.



RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

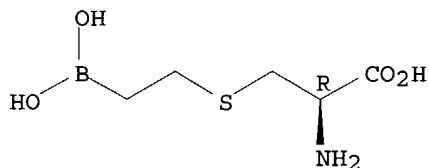
Absolute stereochemistry.



RN 222638-67-7 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT 194656-75-2P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

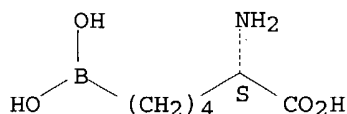
(preparation, arginase inhibitory activity, and crystal structure of)

RN 194656-75-2 CAPLUS

CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)



Absolute stereochemistry.



● HCl

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:489955 CAPLUS  
DOCUMENT NUMBER: 135:223271  
TITLE: Classical and Slow-Binding Inhibitors of Human Type II Arginase  
AUTHOR(S): Colleluori, Diana M.; Ash, David E.  
CORPORATE SOURCE: Department of Biochemistry, Temple University School of Medicine, Philadelphia, PA, 19140, USA  
SOURCE: Biochemistry (2001), 40(31), 9356-9362  
CODEN: BICHAW; ISSN: 0006-2960  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Arginases catalyze the hydrolysis of L-arginine to yield L-ornithine and urea. Recent studies indicate that arginases, both the type I and type II isoenzymes, participate in the regulation of nitric oxide production by modulating the availability of arginine for nitric oxide synthase. Due to the reciprocal regulation between arginase and nitric oxide synthase, arginase inhibitors have therapeutic potential in treating nitric oxide-dependent smooth muscle disorders, such as erectile dysfunction. The authors demonstrate the competitive inhibition of the mitochondrial human type II arginase by N $\omega$ -hydroxy-L-arginine, the intermediate in the reaction catalyzed by nitric oxide synthase, and its analog N $\omega$ -hydroxy-nor-L-arginine, with K<sub>i</sub> values of 1.6  $\mu$ M and 51 nM at pH 7.5, resp. The authors also demonstrate the inhibition of human type II arginase by the boronic acid-based transition-state analogs 2(S)-amino-6-boronoheptanoic acid (ABH) and S-(2-boronoethyl)-L-cysteine (BEC), which are known inhibitors of type I arginase. At pH 7.5, both ABH and BEC are classical, competitive inhibitors of human type II arginase with K<sub>i</sub> values of 0.25 and 0.31  $\mu$ M, resp. However, at pH 9.5, ABH and BEC are slow-binding inhibitors of the enzyme with K<sub>i</sub> values of 8.5 and 30 nM, resp. The findings presented here indicate that the design of arginine analogs with uncharged, tetrahedral functional groups will lead to the development of more potent inhibitors of arginases at physiol. pH.

IT 222638-65-5

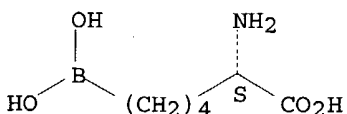
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(arginine analogs as classical and slow-binding inhibitors of human type II arginase)

RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



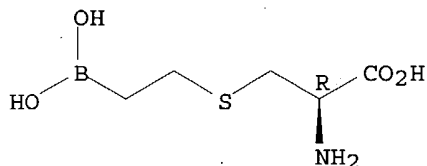
IT 63107-40-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(arginine analogs as classical and slow-binding inhibitors of human type II arginase)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:78738 CAPLUS

DOCUMENT NUMBER: 134:261208

TITLE: Probing Erectile Function: S-(2-Boronoethyl)-L-Cysteine Binds to Arginase as a Transition State Analogue and Enhances Smooth Muscle Relaxation in Human Penile Corpus Cavernosum

AUTHOR(S): Kim, Noel N.; Cox, J. David; Baggio, Ricky F.; Emig, Frances A.; Mistry, Sanjay K.; Harper, Sandy L.; Speicher, David W.; Morris, Sidney M., Jr.; Ash, David E.; Traish, Abdulmageed; Christianson, David W.

CORPORATE SOURCE: Departments of Urology and Biochemistry, Boston University School of Medicine, Boston, MA, 02118, USA

SOURCE: Biochemistry (2001), 40(9), 2678-2688

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The boronic acid-based arginine analog S-(2-boronoethyl)-L-cysteine (BEC) has been synthesized and assayed as a slow-binding competitive inhibitor of the binuclear manganese metalloenzyme arginase. Kinetic measurements indicate a KI value of 0.4-0.6  $\mu$ M, which is in reasonable agreement with the dissociation constant of 2.22  $\mu$ M measured by isothermal titration calorimetry. The x-ray crystal structure of the arginase-BEC complex has been determined at 2.3 Å resolution from crystals perfectly twinned by hemihedry. The structure of the complex reveals that the boronic acid moiety undergoes nucleophilic attack by metal-bridging hydroxide ion to yield a tetrahedral boronate anion that bridges the binuclear manganese cluster, thereby mimicking the tetrahedral intermediate (and its flanking transition states) in the arginine hydrolysis reaction. Accordingly, the binding mode of BEC is consistent with the structure-based mechanism proposed for arginase as outlined in Cox et al. [Cox, J. D., Cama, E., Colletuori D. M., Pethe, S., Boucher, J. S., Mansuy, D., Ash, D. E., and Christianson, D. W. (2001) Biochem. 40]. Since BEC does not inhibit nitric oxide synthase, BEC serves as a valuable reagent to probe the physiol. relation between arginase and nitric oxide (NO) synthase in regulating the NO-dependent smooth muscle relaxation in human penile corpus cavernosum tissue that is required for erection. Consequently, the authors demonstrate that arginase is present in human penile corpus cavernosum tissue, and that the arginase inhibitor BEC causes significant enhancement of NO-dependent smooth muscle relaxation in this tissue. Therefore, human penile arginase is a potential target for the treatment of sexual dysfunction in the male.

IT 63107-40-4P

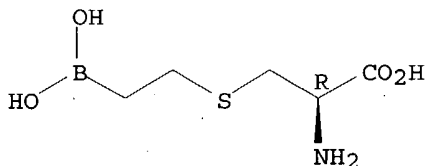
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(boronoethylcysteine binds to arginase as a transition state analog and enhances smooth muscle relaxation in human penile corpus cavernosum in relation to probing erectile function and treatment of sexual dysfunction)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:13532 CAPLUS

DOCUMENT NUMBER: 132:322102

TITLE: Synthesis and evaluation of  $\omega$ -borono- $\alpha$ -amino acids as active-site probes of arginase and nitric oxide synthases

AUTHOR(S): Collet, Sylvain; Carreaux, Francois; Boucher, Jean-Luc; Pethe, Stephanie; Lepoivre, Michel; Danion-Bougot, Renee; Danion, Daniel

CORPORATE SOURCE: UMR 6510 CNRS, Synthèse et Electrosynthèse organiques, Université Rennes I, Rennes, 35042, Fr.

SOURCE: Perkin 1 (2000), (2), 177-182

CODEN: PERKF9

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Enantiomerically pure  $\omega$ -borono- $\alpha$ -amino acids of various chain lengths have been synthesized according to a general methodol. involving condensation of alkenyl and alkynyl bromides with NiII complex of the Schiff base derived from glycine and (S)-2-[N'-(N-benzylpropyl)amino]benzophenone, hydroboration of the intermediate  $\omega$ -unsatd.  $\alpha$ -amino acids with diisopinocampheylborane, oxidation with acetaldehyde. Some of these compds. act as potent inhibitors of rat liver and murine macrophage arginases, demonstrating that distance between the B(OH)<sub>2</sub> and  $\alpha$ -amino acid groups is a key determinant for their interaction with arginase. In contrast, they are without effect on neuronal and inducible NO synthases.

IT 222638-65-5P

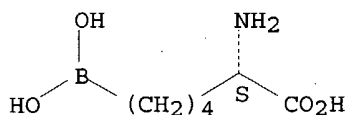
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and evaluation of enantiopure  $\omega$ -borono- $\alpha$ -amino acids as inhibitors of arginase and nitric oxide synthases)

RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

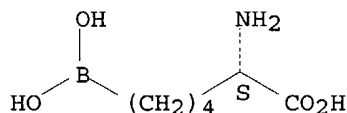
Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1999:799941 CAPLUS  
 DOCUMENT NUMBER: 132:148344  
 TITLE: A New Chromophoric Assay for Arginase Activity  
 AUTHOR(S): Baggio, Rick; Cox, J. David; Harper, Sandy L.;  
 Speicher, David W.; Christianson, David W.  
 CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of  
 Chemistry, University of Pennsylvania, Philadelphia,  
 PA, 19104-6323, USA  
 SOURCE: Analytical Biochemistry (1999), 276(2), 251-253  
 CODEN: ANBCA2; ISSN: 0003-2697  
 PUBLISHER: Academic Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB It is reported that 1-nitro-3-guanidinobenzene (NGB) is a new assay  
 substrate for arginase, yielding products urea plus the chromophore  
 m-nitroaniline. The simple two-step synthesis of NGB is outlined. The  
 authors concluded with a description of its kinetic parameters and a brief  
 discussion of the utility of this assay. (c) 1999 Academic Press.  
 IT 222638-65-5  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); BIOL (Biological study)  
 (chromophoric assay for arginase activity using nitroguanidinobenzene  
 as substrate and study of enzyme inhibition by aminoboronoheptanoic  
 acid)  
 RN 222638-65-5 CAPLUS  
 CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1999:725889 CAPLUS  
 DOCUMENT NUMBER: 132:76677  
 TITLE: Arginase-boronic acid complex highlights a  
 physiological role in erectile function  
 AUTHOR(S): Cox, J. David; Kim, Noel N.; Traish, Abdulmageed M.;  
 Christianson, David W.  
 CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of  
 Chemistry, University of Pennsylvania, Philadelphia,  
 PA, 19104-6323, USA  
 SOURCE: Nature Structural Biology (1999), 6(11), 1043-1047  
 CODEN: NSBI EW; ISSN: 1072-8368  
 PUBLISHER: Nature America  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The crystal structure of the complex between the binuclear manganese

metalloenzyme arginase and the boronic acid analog of L-arginine, 2(S)-amino-6-borono-hexanoic acid (ABH), has been determined at 1.7 Å resolution from a crystal perfectly twinned by hemihedry. ABH binds as the tetrahedral boronate anion, with one hydroxyl oxygen sym. bridging the binuclear manganese cluster and a second hydroxyl oxygen coordinating to Mn2+A. This binding mode mimics the transition state of a metal-activated hydroxide mechanism. This transition state structure differs from that occurring in NO biosynthesis, thereby explaining why ABH does not inhibit NO synthase. We also show that arginase activity is present in the penis. Accordingly, the tight binding and specificity of ABH allows us to probe the physiol. role of arginase in modulating the NO-dependent smooth muscle relaxation required for erection. Strikingly, ABH causes significant enhancement of nonadrenergic, noncholinergic nerve-mediated relaxation of penile corpus cavernosum smooth muscle, suggesting that arginase inhibition sustains L-arginine concns. for NO synthase activity. Therefore, human penile arginase is a potential target for therapeutic intervention in the treatment of erectile dysfunction.

IT 222638-65-5D, arginase complexes

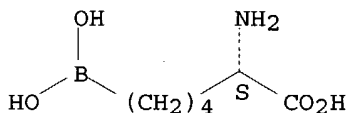
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(arginase-boronic acid complex highlights a physiol. role in erectile function)

RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:547966 CAPLUS

DOCUMENT NUMBER: 131:295396

TITLE: Biochemical and functional profile of a newly developed potent and isozyme-selective arginase inhibitor

AUTHOR(S): Baggio, Ricky; Emig, Frances A.; Christianson, David W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish

CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (1999), 290(3), 1409-1416

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An increase in arginase activity has been associated with the pathophysiol. of a number of conditions, including an impairment in nonadrenergic and noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal smooth muscle. An arginase inhibitor may rectify this condition. We compared the effects of a newly designed arginase inhibitor, 2(S)-amino-6-borono-hexanoic acid (ABH), with the currently available Nω-hydroxy-L-arginine (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS) smooth-muscle relaxation and the arginase activity in the IAS and other tissues. Arginase caused an attenuation of the IAS smooth-muscle relaxations by NANC nerve stimulation that was

restored by the arginase inhibitors. L-HO-Arg but not ABH caused dose-dependent and complete reversal of N $\omega$ -nitro-L-arginine-suppressed IAS relaxation that was similar to that seen with L-arginine. Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated relaxation of the IAS. In the IAS, ABH was found to be  $\approx$ 250 times more potent than L-HO-Arg in inhibiting the arginase activity. L-HO-Arg was found to be 10 to 18 times more potent in inhibiting the arginase activity in the liver than in nonhepatic tissues. We conclude that arginase plays a significant role in the regulation of nitric oxide synthase-mediated NANC relaxation in the IAS. The advent of new and selective arginase inhibitors may play a significant role in the discrimination of arginase isoenzymes and have important pathophysiol. and therapeutic implications in gastrointestinal motility disorders.

IT 222638-65-5

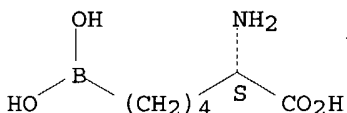
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(biochem. and functional profile of potent and isoenzyme-selective arginase inhibitor, 2(S)-amino-6-boronoheptanoic acid)

RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:271330 CAPLUS

DOCUMENT NUMBER: 130:282369

TITLE: Preparation of borono amino acids as arginase inhibitors

INVENTOR(S): Christianson, David W.; Baggio, Ricky; Elbaum, Daniel

PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA

SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919295	A1	19990422	WO 1998-US21430	19981009
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2305703	AA	19990422	CA 1998-2305703	19981009
AU 9897979	A1	19990503	AU 1998-97979	19981009
EP 1049660	A1	20001108	EP 1998-952229	19981009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6387890	B1	20020514	US 2000-545737	20000410
US 2003036529	A1	20030220	US 2002-53939	20020123
US 6723710	B2	20040420		
US 2004063666	A1	20040401	US 2003-661965	20030912
PRIORITY APPLN. INFO.:			US 1997-61607P	P 19971010
			WO 1998-US21430	W 19981009

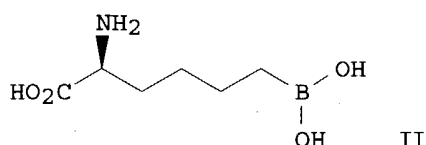
US 2000-545737 A3 20000410

US 2002-53939 A1 20020123

OTHER SOURCE(S) :

MARPAT 130:282369

GI



AB Title compds. HO<sub>2</sub>CCH(NH<sub>2</sub>)-Y<sub>1</sub>-Y<sub>2</sub>-Y<sub>3</sub>-Y<sub>4</sub>-B(OH)<sub>2</sub> (I; Y<sub>1</sub>-Y<sub>4</sub> = independently CH<sub>2</sub>, S, O, NH, N-alkyl; with the proviso that Y<sub>2</sub> ≠ S when Y<sub>1</sub> = Y<sub>3</sub> = Y<sub>4</sub> = CH<sub>2</sub>) are described. Compns. and methods for inhibiting arginase activity using I, including arginase activity in a mammal, are provided. Methods of making the compns. of the invention are also provided as are methods of using the compns. therapeutically. Thus, borono amino acid II, prepared in 5 steps from Boc-Glu-OCMe<sub>3</sub> via conversion to the side chain aldehyde, Wittig olefination with Ph<sub>3</sub>P:CH<sub>2</sub>, hydroboration with BH<sub>3</sub>, trapping with (1S,2S,4R,6S)-(+)-pinanediol, and deprotection with BCl<sub>3</sub>, inhibited arginase with K<sub>i</sub> = 0.1 μM.

IT 194656-75-2P

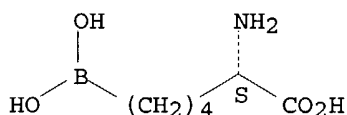
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of borono amino acids as arginase inhibitors)

RN 194656-75-2 CAPLUS

CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT 63107-40-4P 222638-65-5P 222638-67-7P

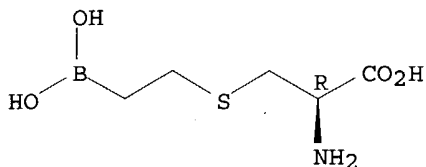
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of borono amino acids as arginase inhibitors)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

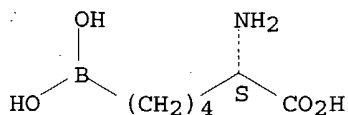
Absolute stereochemistry.



RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

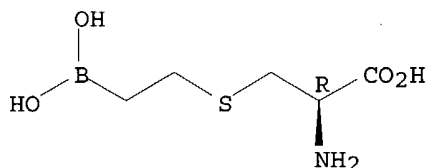
Absolute stereochemistry.



RN 222638-67-7 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:528761 CAPLUS

DOCUMENT NUMBER: 127:201930

TITLE: Inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of a transition state analog inhibitor, 2(S)-amino-6-boronohexanoic acid

AUTHOR(S): Baggio, Ricky; Elbaum, Daniel; Kanyo, Zoltan F.; Carroll, Patrick J.; Cavalli, R. Christopher; Ash, David E.; Christianson, David W.

CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA

SOURCE: Journal of the American Chemical Society (1997), 119(34), 8107-8108

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The tetrahedral borate anion is a modest inhibitor of Mn<sup>2+</sup>-arginase, a critical metalloenzyme of mammalian nitrogen metabolism The crystal structure of

the arginase-ornithine-borate complex reveals the net displacement of the solvent mol. bridging the binuclear manganese cluster by a borate oxygen atom in the native enzyme active site. Since this binding mode is reminiscent of the tetrahedral intermediate proposed for arginase-catalyzed arginine hydrolysis, it is postulated that a boronic acid-based arginine isostere would bind to arginase as the tetrahedral boronate anion and therefore mimic the tetrahedral intermediate and its flanking transition states in catalysis. Arginine isostere 2(S)-amino-6-boronohexanoic acid (I) was synthesized and evaluated for inhibition of arginase-catalyzed arginine hydrolysis. The results indicate that I is one of the most potent reversible inhibitors of arginase known to date with IC<sub>50</sub> = 0.8 μM. Complete kinetic characterization of I is complicated by nonlinearity of unknown origin (there is no evidence for slow-binding behavior), but competition binding



expts. with N-hydroxyarginine indicate that  $K_d \leq 0.1 \mu M$ . Based on anal. of the crystal structure of the arginase-ornithine-borate complex, a possible binding mode for I is postulated in which the metal-bridging solvent mol. observed in the native enzyme is displaced by an oxygen atom of the tetrahedral boronic acid anion.

IT 194656-75-2P

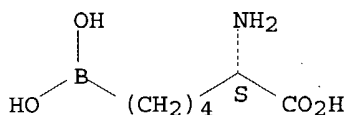
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(inhibition of  $Mn^{2+}$ -arginase by borate leads to the design of 2(S)-amino-6-borono-hexanoic acid as a transition state analog inhibitor)

RN 194656-75-2 CAPLUS

CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L4 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1977:406321 CAPLUS

DOCUMENT NUMBER: 87:6321

TITLE: Preparation and evaluation of immunoglobulins labeled with S-(2-boronoethyl)cysteine

AUTHOR(S): Hartz, Thomas Peter, Jr.

CORPORATE SOURCE: Memphis State Univ., Memphis, TN, USA

SOURCE: (1976) 87 pp. Avail.: Xerox Univ. Microfilms, Ann Arbor, Mich., Order No. 77-3150

From: Diss. Abstr. Int. B 1977, 37(8), 3927-8

DOCUMENT TYPE: Dissertation

LANGUAGE: English

AB Unavailable

IT 63107-40-4P

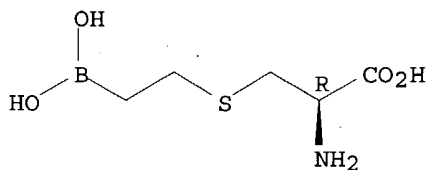
RL: SPN (Synthetic preparation); PREP (Preparation)

(labeling of immunoglobulins with, preparation and evaluation of)

RN 63107-40-4 CAPLUS

CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

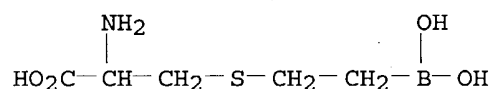
ACCESSION NUMBER: 1964:461710 CAPLUS

DOCUMENT NUMBER: 61:61710

ORIGINAL REFERENCE NO.: 61:10696b-d

TITLE: Synthesis and biological evaluation of water-soluble 2-borono-ethylthio compounds

AUTHOR(S): Matteson, D. S.; Soloway, A. H.; Tomlinson, D. W.;  
Campbell, J. D.; Nixon, G. A.  
CORPORATE SOURCE: Washington State Univ., Pullman  
SOURCE: Journal of Medicinal Chemistry (1964), 7(5), 640-3  
CODEN: JMCMAR; ISSN: 0022-2623  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable  
OTHER SOURCE(S): CASREACT 61:61710  
AB The radical-catalyzed addition of mercaptans to the double bond of di-Bu  
ethyleneboronate has been employed for the synthesis of several water-soluble  
boronic acids. Adducts have been obtained with mercaptoacetic acid,  
β-mercaptopropionic acid, mercaptosuccinic acid, mercaptoethylamine  
hydrochloride, cysteine, mercaptoethanol, and NaHSO<sub>3</sub>. The  
2-mercaptopyrimidine adduct could not be obtained directly but was prepared  
from di-Bu mercaptoethaneboronate and 2-chloropyrimidine. The boronic  
acids have been tested in C<sub>3</sub>H mice with subcutaneously implanted brain  
tumors to determine the ratio of B in the tumor to that in brain, blood, and  
muscle, as a function of time. One of the more favorable compds. on this  
basis was S-boronoethylcysteine. High transient boron ratios were found  
to be inadequate, and the need for binding compds. to tumor with  
concomitantly low B concns. in blood and brain is discussed.  
IT 88642-86-8, Alanine, 3-[(2-boronoethyl)thio]-  
(preparation of)  
RN 88642-86-8 CAPLUS  
CN Alanine, 3-[(2-boronoethyl)thio]- (7CI) (CA INDEX NAME)



=> file beilstein  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
65.55	232.55

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

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ENTRY	SESSION
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FILE RELOADED ON OCTOBER 20, 2002  
FILE LAST UPDATED ON MARCH 30, 2004

FILE COVERS 1771 TO 2003.  
\*\*\* FILE CONTAINS 8,932,479 SUBSTANCES \*\*\*

>>> PLEASE NOTE: Reaction data and substance data are stored in  
separate documents and can not be searched together in one  
query.  
Reaction data for BEILSTEIN compounds may be displayed  
immediately with the display codes PRE (preparations) and REA  
(reactions). A substance answer set retrieved after the search  
for a chemical name, a molecular formula or a structure search  
for example can be restricted to compounds with available  
reaction information by concatenation with PRE/FA, REA/FA or  
more general with RX/FA. The BEILSTEIN Registry Number (BRN)  
is the link between a BEILSTEIN compound and belonging reactions.

For more detailed reaction searches BRNs can be selected from substance answer sets and searched in the next step as reaction partner BRNs - Reactant (RX.RBRN) or Product BRN (RX.PBRN). After a search for reaction details substance documents associated with reactants or products may be retrieved by searching RX.PBRNs or RX.RBRNs as BRNs. <<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

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* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE    *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                  *
* FOR PRICE INFORMATION SEE HELP COST                          *
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FILE 'REGISTRY' ENTERED AT 12:20:29 ON 26 APR 2004

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L3          5 S L1 FULL
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FILE 'CAPLUS' ENTERED AT 12:22:51 ON 26 APR 2004

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L4          14 S L3
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FILE 'BEILSTEIN' ENTERED AT 12:23:25 ON 26 APR 2004

=> s l1 full

FULL SEARCH INITIATED 12:23:32 FILE 'BEILSTEIN'

FULL SCREEN SEARCH COMPLETED - 93 TO ITERATE

100.0% PROCESSED 93 ITERATIONS

3 ANSWERS

SEARCH TIME: 00.00.05

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L5          3 SEA SSS FUL L1
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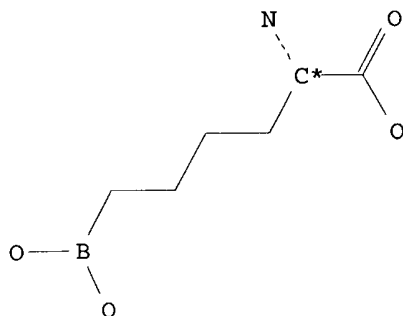
L5 ANSWER 1 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

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                                acid hydrochloride
Fragm. Molec. Formula (FMF):  C6 H14 B N O4 , Cl H
Molecular Formula (MF):       C6 H14 B N O4 . Cl H
Molecular Weight (MW):        174.99, 36.46
Fragment BRN (FBRN):          8486411, 1098214
Lawson Number (LN):           3808
File Segment (FS):            Stereo compound
Compound Type (CTYPE):        acyclic
Constitution ID (CONSID):      7217850
Tautomer ID (TAUTID):          8016642
Entry Date (DED):             2000/07/18
Update Date (DUPD):           2000/07/18
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CM 1

FBRN 8486411

FMF C6 H14 B N O4



CM 2

FBRN 1098214

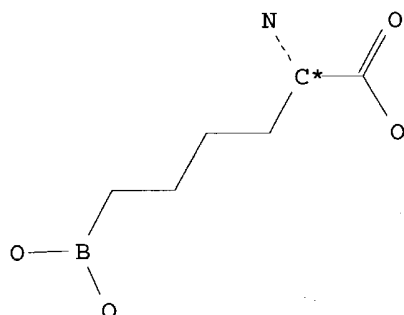
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Field Availability:

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FBRN	Fragment BRN	2
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FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
MP	Melting Point	1
NMR	Nuclear Magnetic Resonance	3

L5 ANSWER 2 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN): 8486411  
Chemical Name (CN): (S)-2-Amino-6-(dihydroxyboryl)hexanoic acid  
Molec. Formula (MF): C6 H14 B N O4  
Molecular Weight (MW): 174.99  
Lawson Number (LN): 3808  
File Segment (FS): Stereo compound  
Compound Type (CTYPE): acyclic  
Constitution ID (CONSID): 7193885  
Tautomer ID (TAUTID): 8001997  
Entry Date (DED): 2000/07/18  
Update Date (DUPD): 2000/07/18



Field Availability:

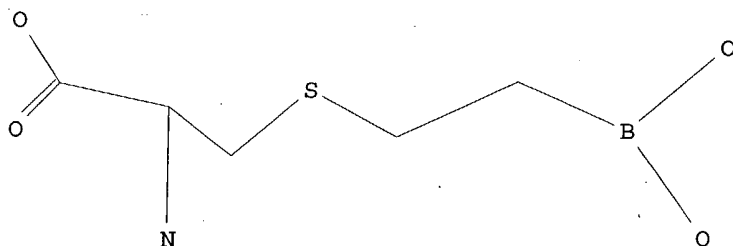
Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	1
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
MP	Melting Point	1
NMR	Nuclear Magnetic Resonance	2
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

L5 ANSWER 3 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN): 4132291  
 CAS Reg. No. (RN): 63107-40-4, 88642-86-8  
 Chemical Name (CN): S-(2-Borono-aethylthio)-cysteine  
 Molec. Formula (MF): C5 H12 B N O4 S  
 Molecular Weight (MW): 193.02  
 Lawson Number (LN): 3813, 3544  
 Compound Type (CTYPE): acyclic  
 Constitution ID (CONSID): 3711429  
 Tautomer ID (TAUTID): 3982454  
 Beilstein Citation (BSO): 5-04  
 Entry Date (DED): 1991/03/19  
 Update Date (DUPD): 1994/12/21



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
RN	CAS Registry Number	2
CN	Chemical Name	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	2
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
BSO	Beilstein Citation	1
ED	Entry Date	1
UPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

=> d frxpro 1-2

L5 ANSWER 1 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

L5 ANSWER 2 OF 3 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Reaction:

RX

Reaction ID (.ID): 5352744  
 Reactant BRN (.RBRN): 8516325  
 Reactant (.RCT): (S)-2-(tert-Butoxycarbonylamino)-6-  
 <(1S,2S,3R,5S)-(+)-pinanyl-2,3-  
 dioxyboryl>hexanoic acid methyl ester  
 Product BRN (.PBRN): 8486411  
 Product (.PRO): (S)-2-Amino-6-(dihydroxyboryl)hexanoic  
 acid  
 No. of React. Details (.NVAR): 1

Reaction Details:

RX

Reaction RID (.RID): 5352744.1  
 Reaction Classification (.CL): Preparation  
 Yield (.YDT): 79 percent (BRN=8486411)  
 Reagent (.RGT): HCl, H2O  
 Time (.TIM): 2 hour(s)

Temperature (.T): 70 Cel  
Reaction Type (.TYP): Hydrolysis  
Reference(s):

1. Collet, Sylvain; Carreaux, Francois; Boucher, Jean-Luc; Pethe, Stephanie; Lepoivre, Michel; Danion-Bougot, Renee; Danion, Daniel, J.Chem.Soc.Perkin Trans.1, CODEN: JCPRB4(2), <2000>, 177 - 182; BABS-6229491

=> d his

(FILE 'HOME' ENTERED AT 12:16:09 ON 26 APR 2004)

FILE 'REGISTRY' ENTERED AT 12:20:29 ON 26 APR 2004

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 5 S L1 FULL

FILE 'CAPLUS' ENTERED AT 12:22:51 ON 26 APR 2004

L4 14 S L3

FILE 'BEILSTEIN' ENTERED AT 12:23:25 ON 26 APR 2004

L5 3 S L1 FULL

=> s arginase inhib?

2724 ARGINASE  
113 ARGINASES  
2725 ARGINASE  
(ARGINASE OR ARGINASES)

1238571 INHIB?  
L1 132 ARGINASE INHIB?  
(ARGINASE(W) INHIB?)

=> s l1 and cancer

117644 CANCER  
15808 CANCERS  
122270 CANCER  
(CANCER OR CANCERS)

L2 1 L1 AND CANCER

=> d ibib abs

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1984:622236 CAPLUS

DOCUMENT NUMBER: 101:222236

TITLE: **Cancer** therapy with chemically modified  
enzymes. II. The therapeutic effectiveness of  
arginase, and arginase modified by the covalent  
attachment of polyethylene glycol, on the Taper liver  
tumor and the L5178Y murine leukemia

AUTHOR(S): Savoca, K. V.; Davis, F. F.; Van Es, T.; McCoy, J. R.;  
Palczuk, N. C.

CORPORATE SOURCE: Dep. Biol., Rutgers Univ., New Brunswick, NJ, 08903,  
USA

SOURCE: Cancer Biochem. Biophys. (1984), 7(3), 261-8  
CODEN: CABCD4; ISSN: 0305-7232

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Monomethoxypolyethylene glycol (PEG) was attached covalently to arginase;  
PEG-arginase was effective in prolonging the survival times of mice  
injected with the Taper liver tumor, whereas unmodified arginase was  
ineffective. PEG-arginase was more effective than arginase in the in  
vitro destruction of L5178Y mouse leukemia. However, neither PEG-arginase  
nor **arginase inhibited** the in vivo growth of this  
tumor.

=> s arginase and cancer

2724 ARGINASE  
113 ARGINASES  
2725 ARGINASE  
(ARGINASE OR ARGINASES)

117644 CANCER  
15808 CANCERS  
122270 CANCER  
(CANCER OR CANCERS)

L3 41 ARGINASE AND CANCER

=> d scan

L3 41 ANSWERS CAPLUS COPYRIGHT 2000 ACS

IC ICM A61K038-50

ICS A61K049-00; C12N009-78; C12Q001-34



CC 1-12 (Pharmacology)

TI Amino acid degrading enzymes modulate cell death

ST amino acid degrading enzyme cell death modulation; cytoprotectant amino acid degrading enzyme; TNF amino acid degrading enzyme antitumor

IT Antitumor agents  
 Cytoprotective agents  
 Neuroglia  
 (amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

IT Tumor necrosis factors  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

IT Gene, animal  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (amino acid-degrading enzyme-encoding, transfection of; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

IT Enzymes, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (amino acid-degrading; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

IT Amino acids, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (enzymes degrading; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

IT Cytoprotective agents  
 (neuroprotectants; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

IT Transformation, genetic  
 (of amino acid-degrading enzyme genes; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

IT Drug screening  
 (of amino acid-degrading enzyme-affecting compds.; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

IT Gene therapy  
 (with amino acid-degrading enzyme genes; amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

IT 9000-96-8, **Arginase** 9015-68-3, Asparaginase 9024-77-5, Arginine decarboxylase 9027-98-9  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (amino acid degrading enzymes modulate cell death in relation to cytoprotectant activity and potentiation of antitumor activity of TNF $\alpha$  and inhibition of protein synthesis)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d ti 1-10

L3 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI **Arginase** activity in human breast **cancer** cell lines:  
Nω-hydroxy-L-arginine selectively inhibits cell proliferation and  
induces apoptosis in MDA-MB-468 cells

L3 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI Immunohistochemical study of **arginase** in **cancer** of the  
stomach

L3 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI Evaluation of serum **arginase** activity in benign prostatic  
hypertrophy and prostatic **cancer**

L3 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI Amino acid degrading enzymes modulate cell death

L3 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI Human **arginase** II cDNA sequence, recombinant production, and use  
for gene therapy and clinical diagnosis

L3 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI Metabolic capacity for l-citrulline synthesis from ammonia in rat isolated  
colonocytes

L3 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI Growth inhibitory effect of L-canavanine against MIA PaCa-2 pancreatic  
**cancer** cells is not due to conversion to its toxic metabolite  
canaline

L3 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI Applications of electron paramagnetic resonance spectroscopy to study  
interactions of iron proteins in cells with nitric oxide

L3 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI Use of a non-mammalian DNA virus to express an exogenous gene in a  
mammalian cell for gene therapy in treatment of gene deficiency disorder  
or liver **cancer**

L3 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2000 ACS

TI Extracorporeal blood treatment for systemic deprivation of amino acids in  
treatment of **cancer**

=> d ibib abs 2

L3 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:173162 CAPLUS  
Correction of: 1996:636792

DOCUMENT NUMBER: 132:178950  
Correction of: 125:324820

TITLE: Immunohistochemical study of **arginase** in  
**cancer** of the stomach

AUTHOR(S): Wu, Chew Wun; Chung, Wen Wei; Chi, Chin-Wen; Kao, Hwa  
Li; Lui, Wing Yiu; Peng, Fang-Ku; Wang, Soo Ray

CORPORATE SOURCE: Veterans General Hospital, National Yang-Ming  
University, Taipei, 11217, Taiwan

SOURCE: Virchows Arch. (1996), 428(6), 325-331

PUBLISHER: Springer  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB High levels of **arginase** have been detected in gastric adenocarcinoma. To examine the hypothesis that this is due to macrophage infiltration into the tumor, the cellular distribution of **arginase** was localized by immunohistochem. staining. Gastric adenocarcinomas and their corresponding normal tissues (n = 46), leiomyomas (n = 2), leiomyosarcomas (n = 3), human gastric adenocarcinoma cell lines (n = 3), and benign gastric ulcers (n = 4) were examined by the avidin-biotin-peroxidase complex technique. Although macrophages with strong **arginase** immunoreactivity were observed infiltrating both gastric normal and **cancer** tissues, the data suggest the the high **arginase** levels in adenocarcinoma **cancer** tissues originate largely from **cancer** cells.

=> s arginase and (renal or kidney)

2724 ARGINASE  
113 ARGINASES  
2725 ARGINASE  
(ARGINASE OR ARGINASES)  
92639 RENAL  
7 RENALS  
92642 RENAL  
(RENAL OR RENALS)  
177553 KIDNEY  
33592 KIDNEYS  
186263 KIDNEY  
(KIDNEY OR KIDNEYS)  
L4 378 ARGINASE AND (RENAL OR KIDNEY)

=> s l4 and arginase/ti

1155 ARGINASE/TI  
23 ARGINASES/TI  
1173 ARGINASE/TI  
((ARGINASE OR ARGINASES)/TI)  
L5 165 L4 AND ARGINASE/TI

=> d ti 1-10

L5 ANSWER 1 OF 165 CAPLUS COPYRIGHT 2000 ACS  
TI Human **arginase** II cDNA sequence, recombinant production, and use for gene therapy and clinical diagnosis  
  
L5 ANSWER 2 OF 165 CAPLUS COPYRIGHT 2000 ACS  
TI Preparation of borono amino acids as **arginase** inhibitors  
  
L5 ANSWER 3 OF 165 CAPLUS COPYRIGHT 2000 ACS  
TI Expression of **arginase** II and related enzymes in the rat small intestine and **kidney**  
  
L5 ANSWER 4 OF 165 CAPLUS COPYRIGHT 2000 ACS  
TI Immunohistochemical localization of **arginase** II and other enzymes of arginine metabolism in rat **kidney** and liver  
  
L5 ANSWER 5 OF 165 CAPLUS COPYRIGHT 2000 ACS  
TI Identification of two **arginase** isoenzyme activities along the nephron of Meriones shawi

L5 ANSWER 6 OF 165 CAPLUS COPYRIGHT 2000 ACS  
 TI Various changes in nitric oxide synthase and **arginase** II in rat  
**kidney** caused by inorganic mercury

L5 ANSWER 7 OF 165 CAPLUS COPYRIGHT 2000 ACS  
 TI **Arginase** activity and manganese content in various tissues from  
 control and DOCA salt-hypertensive male Sprague Dawley rats

L5 ANSWER 8 OF 165 CAPLUS COPYRIGHT 2000 ACS  
 TI The human **arginases** and **arginase** deficiency

L5 ANSWER 9 OF 165 CAPLUS COPYRIGHT 2000 ACS  
 TI Molecular cloning of cDNA for nonhepatic **arginase** (  
**arginase** II) and comparison of its induction with NO synthase in a  
 murine macrophage-like cell line

L5 ANSWER 10 OF 165 CAPLUS COPYRIGHT 2000 ACS  
 TI **Arginase** activity is modulated by IL-4 and HOArg in nephritic  
 glomeruli and mesangial cells

=> d arginase and erectile

'ARGINASE' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'  
 'AND' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'  
 'ERECTILE' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS ----- GI and AB  
 ALL ----- BIB, AB, IND, RE  
 APPS ----- AI, PRAI  
 BIB ----- AN, plus Bibliographic Data and PI table (default)  
 CAN ----- List of CA abstract numbers without answer numbers  
 CBIB ----- AN, plus Compressed Bibliographic Data  
 DALL ----- ALL, delimited (end of each field identified)  
 DMAX ----- MAX, delimited for post-processing  
 FAM ----- AN, PI and PRAI in table, plus Patent Family data  
 FBIB ----- AN, BIB, plus Patent FAM  
 IND ----- Indexing data  
 IPC ----- International Patent Classifications  
 MAX ----- ALL, plus Patent FAM, RE  
 PATS ----- PI, SO  
 SAM ----- CC, SX, TI, ST, IT  
 SCAN ----- CC, SX, TI, ST, IT (random display, no answer numbers;  
 SCAN must be entered on the same line as the DISPLAY,  
 e.g., D SCAN or DISPLAY SCAN)  
 STD ----- BIB, IPC, and NCL

IABS ----- ABS, indented with text labels  
 IALL ----- ALL, indented with text labels  
 IBIB ----- BIB, indented with text labels  
 IMAX ----- MAX, indented with text labels  
 ISTD ----- STD, indented with text labels

OBIB ----- AN, plus Bibliographic Data (original)  
 OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations  
 SIBIB ----- IBIB, no citations

HIT ----- Fields containing hit terms  
 HITIND ----- IC, ICA, ICI, NCL, CC and index field (ST and IT)  
 containing hit terms

HITRN ----- HIT RN and its text modification  
HITSTR ----- HIT RN, its text modification, its CA index name, and  
its structure diagram  
FHITSTR ----- First HIT RN, its text modification, its CA index name, and  
its structure diagram  
KWIC ----- Hit term plus 20 words on either side  
OCC ----- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.  
ENTER DISPLAY FORMAT (BIB):end

=> s arginase and erectile

```

          2724 ARGINASE
          113 ARGINASES
          2725 ARGINASE
              (ARGINASE OR ARGINASES)
          702 ERECTILE
L6         1 ARGINASE AND ERECTILE

```

=> d ti

```

L6  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2000 ACS
TI  Arginase-boronic acid complex highlights a physiological role in
    erectile function

```

=> s arginase and smooth muscle

```

          2724 ARGINASE
          113 ARGINASES
          2725 ARGINASE
              (ARGINASE OR ARGINASES)
        106447 SMOOTH
          220 SMOOTHS
        106642 SMOOTH
              (SMOOTH OR SMOOTHS)
        202740 MUSCLE
          40152 MUSCLES
        210513 MUSCLE
              (MUSCLE OR MUSCLES)
          46944 SMOOTH MUSCLE
              (SMOOTH(W)MUSCLE)
L7         10 ARGINASE AND SMOOTH MUSCLE

```

=> d ti 1-10

```

L7  ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2000 ACS
TI  IL-4 and IL-13 upregulate arginase I expression by cAMP and
    JAK/STAT6 pathways in vascular smooth muscle cells

L7  ANSWER 2 OF 10  CAPLUS  COPYRIGHT 2000 ACS

```

TI Progression of hepatic stellate cell activation is associated with the level of oxidative stress rather than cytokines during CCl4-induced fibrogenesis

L7 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2000 ACS

TI Enzyme immunoassay for autoantibodies to human liver-type **arginase** and its clinical application

L7 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2000 ACS

TI **Arginase**-boronic acid complex highlights a physiological role in erectile function

L7 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2000 ACS

TI Biochemical and functional profile of a newly developed potent and isozyme-selective **arginase** inhibitor

L7 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2000 ACS

TI Preparation of borono amino acids as **arginase** inhibitors

L7 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2000 ACS

TI Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular **smooth muscle** cells. Role in polyamine biosynthesis

L7 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2000 ACS

TI L-Arginine deficiency causes suppression of nonadrenergic noncholinergic nerve-mediated **smooth muscle** relaxation: Role of L-citrulline recycling

L7 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2000 ACS

TI Beneficial circulatory effect of L-arginine

L7 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2000 ACS

TI Identification of a 15 kilodalton actin binding region on gizzard caldesmon probed by chemical cross-linking

=> d ibib abs 4 5 7

L7 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:725889 CAPLUS

DOCUMENT NUMBER: 132:76677

TITLE: **Arginase**-boronic acid complex highlights a physiological role in erectile function

AUTHOR(S): Cox, J. David; Kim, Noel N.; Traish, Abdulmaged M.; Christianson, David W.

CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA

SOURCE: Nat. Struct. Biol. (1999), 6(11), 1043-1047

CODEN: NSBIEW; ISSN: 1072-8368

PUBLISHER: Nature America

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The crystal structure of the complex between the binuclear manganese metalloenzyme **arginase** and the boronic acid analog of L-arginine, 2(S)-amino-6-boronoheptanoic acid (ABH), has been determined at 1.7 Å resolution from a crystal perfectly twinned by hemihedry. ABH binds as the tetrahedral boronate anion, with one hydroxyl oxygen sym. bridging the binuclear manganese cluster and a second hydroxyl oxygen coordinating to Mn2+A. This binding mode mimics the transition state of a metal-activated hydroxide mechanism. This transition state structure differs from that occurring in NO biosynthesis, thereby explaining why ABH does not inhibit

NO synthase. We also show that **arginase** activity is present in the penis. Accordingly, the tight binding and specificity of ABH allows us to probe the physiol. role of **arginase** in modulating the NO-dependent **smooth muscle** relaxation required for erection. Strikingly, ABH causes significant enhancement of nonadrenergic, noncholinergic nerve-mediated relaxation of penile corpus cavernosum **smooth muscle**, suggesting that **arginase** inhibition sustains L-arginine concns. for NO synthase activity. Therefore, human penile **arginase** is a potential target for therapeutic intervention in the treatment of erectile dysfunction.

REFERENCE COUNT: 35  
 REFERENCE(S): (1) Albina, J; J Immunol 1990, V144, P3877 CAPLUS  
 (3) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS  
 (4) Baggio, R; J Pharmacol Exp Ther 1999, V290, P1409 CAPLUS  
 (5) Bewley, M; Structure 1999, V7, P435 CAPLUS  
 (6) Brunger, A; Acta Crystallogr 1998, VD54, P905 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:547966 CAPLUS

DOCUMENT NUMBER: 131:295396

TITLE: Biochemical and functional profile of a newly developed potent and isozyme-selective **arginase** inhibitor

AUTHOR(S): Baggio, Ricky; Emig, Frances A.; Christianson, David W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish

CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA

SOURCE: J. Pharmacol. Exp. Ther. (1999), 290(3), 1409-1416  
 CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An increase in **arginase** activity has been associated with the pathophysiol. of a number of conditions, including an impairment in nonadrenergic and noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal **smooth muscle**. An **arginase** inhibitor may rectify this condition. We compared the effects of a newly designed **arginase** inhibitor, 2(S)-amino-6-borono-hexanoic acid (ABH), with the currently available N $\omega$ -hydroxy-L-arginine (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS) **smooth-muscle** relaxation and the **arginase** activity in the IAS and other tissues. **Arginase** caused an attenuation of the IAS **smooth-muscle** relaxations by NANC nerve stimulation that was restored by the **arginase** inhibitors. L-HO-Arg but not ABH caused dose-dependent and complete reversal of N $\omega$ -nitro-L-arginine-suppressed IAS relaxation that was similar to that seen with L-arginine. Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated relaxation of the IAS. In the IAS, ABH was found to be  $\approx$ 250 times more potent than L-HO-Arg in inhibiting the **arginase** activity. L-HO-Arg was found to be 10 to 18 times more potent in inhibiting the **arginase** activity in the liver than in nonhepatic tissues. We conclude that **arginase** plays a significant role in the regulation of nitric oxide synthase-mediated NANC relaxation in the IAS. The advent of new and selective **arginase** inhibitors may play a significant role in the discrimination of **arginase** isoenzymes and have important pathophysiol. and therapeutic implications in gastrointestinal motility disorders.

REFERENCE COUNT: 43

REFERENCE(S): (1) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS  
 (2) Biancani, P; Gastroenterology 1985, V89, P867 CAPLUS  
 (3) Boucher, J; Biochem Biophys Res Commun 1994, V203, P1614 CAPLUS  
 (4) Buga, G; Am J Physiol 1996, V271, PH1988 CAPLUS  
 (5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:775272 CAPLUS

DOCUMENT NUMBER: 128:73284

TITLE: Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular **smooth muscle** cells. Role in polyamine biosynthesis

AUTHOR(S): Durante, William; Liao, Lan; Peyton, Kelly J.; Schafer, Andrew I.

CORPORATE SOURCE: Houston Veterans Administration Medical Center and the Department of Medicine, Baylor College of Medicine, Houston, TX, 77030, USA

SOURCE: J. Biol. Chem. (1997), 272(48), 30154-30159

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lysophosphatidylcholine (lyso-PC) is a major component of atherogenic lipids that stimulate vascular **smooth muscle** cell (SMC) proliferation. Because cationic amino acids are metabolized to growth-stimulatory polyamines, we examined whether lyso-PC regulates the transcellular transport and metabolism of cationic amino acids by vascular SMC. Treatment of SMC with lyso-PC initially (0-2 h) decreased cationic amino acid uptake, whereas longer exposures (6-24 h) progressively increased transport. Kinetic studies indicated that lyso-PC-induced inhibition was associated with a decrease in affinity for cationic amino acids, but the stimulation was mediated by an increase in transport capacity. Lyso-PC strongly induced the expression of cationic amino acid transporter-2 mRNA while modestly elevating the level of cationic amino acid transporter-1 mRNA. In addition, lyso-PC stimulated intracellular cationic amino acid metabolism by inducing ornithine decarboxylase activity and mRNA expression and also by inducing **arginase** activity in vascular SMC. In contrast, lyso-PC inhibited the catabolism of L-arginine to nitric oxide by blocking inducible nitric oxide synthase expression. Lyso-PC increased markedly the capacity of SMC to generate putrescine, a polyamine, from extracellular L-ornithine and L-arginine. The lyso-PC-mediated increase in the production of putrescine was reversed by NG-methyl-L-arginine, a competitive inhibitor of cationic amino acid transport, or by  $\alpha$ -difluoromethylornithine, an ornithine decarboxylase inhibitor. The formation of putrescine from L-arginine was also prevented by **arginase** inhibitor NG-hydroxy-L-arginine. These results demonstrate that lyso-PC stimulates polyamine synthesis in vascular SMC by inducing the expression of the genes that regulate both the transport and metabolism of cationic amino acids. The actions of lyso-PC in stimulating cationic amino acid uptake and directing their metabolism to growth-stimulatory polyamines while simultaneously inhibiting the synthesis of antiproliferative NO, may contribute to lyso-PC-induced SMC proliferation and atherosclerotic lesion formation.



(FILE 'HOME' ENTERED AT 07:40:40 ON 18 AUG 2000)

FILE 'CAPLUS' ENTERED AT 07:40:47 ON 18 AUG 2000

L1 1 S 127:201930/DN  
SEL RN

FILE 'REGISTRY' ENTERED AT 07:41:47 ON 18 AUG 2000

L2 8 S E1-E8  
L3 1 S NORLEUCINE AND L2

FILE 'CAPLUS' ENTERED AT 07:42:34 ON 18 AUG 2000

=> s l3 and l2

2 L3  
2671 L2  
L4 2 L3 AND L2

=> s l3 and l1

2 L3  
L5 1 L3 AND L1

=> d ibib abs hitstr it

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:528761 CAPLUS

DOCUMENT NUMBER: 127:201930

TITLE: Inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of a transition state analog inhibitor, 2(S)-amino-6-boronohexanoic acid

AUTHOR(S): Baggio, Ricky; Elbaum, Daniel; Kanyo, Zoltan F.; Carroll, Patrick J.; Cavalli, R. Christopher; Ash, David E.; Christianson, David W.

CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA

SOURCE: J. Am. Chem. Soc. (1997), 119(34), 8107-8108

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The tetrahedral borate anion is a modest inhibitor of Mn<sup>2+</sup>-arginase, a critical metalloenzyme of mammalian nitrogen metabolism The crystal structure of

the arginase-ornithine-borate complex reveals the net displacement of the solvent mol. bridging the binuclear manganese cluster by a borate oxygen atom in the native enzyme active site. Since this binding mode is reminiscent of the tetrahedral intermediate proposed for arginase-catalyzed arginine hydrolysis, it is postulated that a boronic acid-based arginine isostere would bind to arginase as the tetrahedral boronate anion and therefore mimic the tetrahedral intermediate and its flanking transition states in catalysis. Arginine isostere 2(S)-amino-6-boronohexanoic acid (I) was synthesized and evaluated for inhibition of arginase-catalyzed arginine hydrolysis. The results indicate that I is one of the most potent reversible inhibitors of arginase known to date with IC<sub>50</sub> = 0.8 μM. Complete kinetic characterization of I is complicated by nonlinearity of unknown origin (there is no evidence for slow-binding behavior), but competition binding expts. with N-hydroxyarginine indicate that K<sub>d</sub> ≤ 0.1 μM. Based on anal. of the crystal structure of the arginase-ornithine-borate complex, a possible binding mode for I is postulated in which the

metal-bridging solvent mol. observed in the native enzyme is displaced by an oxygen atom of the tetrahedral boronic acid anion.

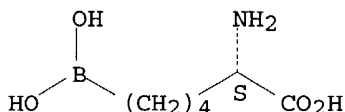
IT 194656-75-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

RN 194656-75-2 CAPLUS

CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT Enzyme inhibition kinetics

Transition state structure

(inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 24277-39-2

RL: RCT (Reactant)

(borohydride reduction during chemical synthesis; inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 11129-12-7D, Borate, complex with arginase and ornithine

RL: PRP (Properties)

(crystal structure; inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 194656-75-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 9000-96-8, Arginase

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 90194-99-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and Swern oxidation during chemical synthesis; inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 194656-74-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and deprotection during chemical synthesis; inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

IT 145037-74-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and hydroboration and protection during chemical synthesis;

inhibition of  $Mn^{2+}$ -arginase by borate leads to the design of  
2(S)-amino-6-borono-hexanoic acid as a transition state analog  
inhibitor)

IT 194656-73-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and reaction with triphenylphosphonium methylide during

chemical

synthesis; inhibition of  $Mn^{2+}$ -arginase by borate leads to the design  
of 2(S)-amino-6-borono-hexanoic acid as a transition state analog  
inhibitor)

=> s 127:201930/dn

L1 1 127:201930/DN

=> d

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS  
AN 1997:528761 CAPLUS  
DN 127:201930  
TI Inhibition of Mn2+2-arginase by borate leads to the design of a transition state analog inhibitor, 2(S)-amino-6-boronohexanoic acid  
AU Baggio, Ricky; Elbaum, Daniel; Kanyo, Zoltan F.; Carroll, Patrick J.; Cavalli, R. Christopher; Ash, David E.; Christianson, David W.  
CS Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA  
SO J. Am. Chem. Soc. (1997), 119(34), 8107-8108  
CODEN: JACSAT; ISSN: 0002-7863  
PB American Chemical Society  
DT Journal  
LA English

=> d it

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS  
IT Enzyme inhibition kinetics  
Transition state structure  
(inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)  
IT 24277-39-2  
RL: RCT (Reactant)  
(borohydride reduction during chemical synthesis; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)  
IT 11129-12-7D, Borate, complex with arginase and ornithine  
RL: PRP (Properties)  
(crystal structure; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)  
IT 194656-75-2P  
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)  
IT 9000-96-8, Arginase  
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)  
IT 90194-99-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and Swern oxidation during chemical synthesis; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)  
IT 194656-74-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(preparation and deprotection during chemical synthesis; inhibition of Mn2+2-arginase by borate leads to the design of 2(S)-amino-6-

boronohexanoic acid as a transition state analog inhibitor)

IT 145037-74-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and hydroboration and protection during chemical synthesis;  
 inhibition of Mn2+2-arginase by borate leads to the design of  
 2(S)-amino-6-boronohexanoic acid as a transition state analog  
 inhibitor)

IT 194656-73-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and reaction with triphenylphosphonium methyllide during  
 chemical synthesis; inhibition of Mn2+2-arginase by borate leads to the design  
 of 2(S)-amino-6-boronohexanoic acid as a transition state analog  
 inhibitor)

=> sel rn

E1 THROUGH E8 ASSIGNED

=> file reg

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 for details.

=> s e1-e8

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1 145037-74-7/BI
  (145037-74-7/RN)
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  (194656-74-1/RN)
1 194656-75-2/BI
  (194656-75-2/RN)
1 24277-39-2/BI
  (24277-39-2/RN)
1 9000-96-8/BI
  (9000-96-8/RN)
1 90194-99-3/BI
  (90194-99-3/RN)
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    -99-3/BI)

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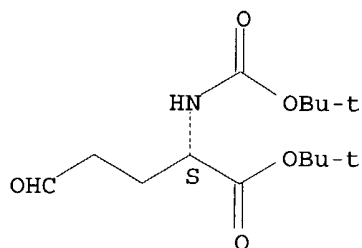
L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Arginase (9CI)  
MF Unspecified  
CI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

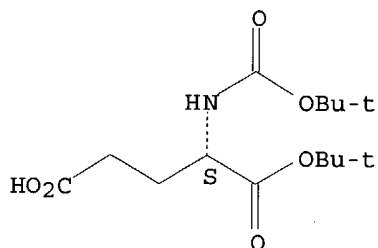
L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN L-Norvaline, N-[(1,1-dimethylethoxy)carbonyl]-5-oxo-, 1,1-dimethylethyl ester (9CI)  
MF C14 H25 N O5

Absolute stereochemistry.



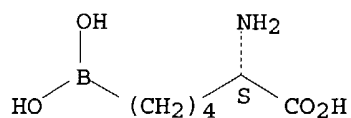
L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-, 1-(1,1-dimethylethyl) ester (9CI)  
MF C14 H25 N O6  
CI COM

Absolute stereochemistry. Rotation (-).



L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN L-Norleucine, 6-borono-, hydrochloride (9CI)  
MF C6 H14 B N O4 . Cl H

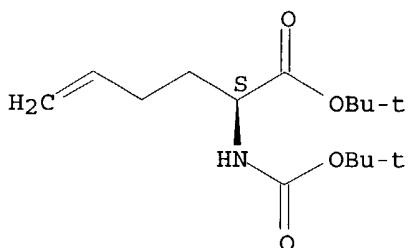
Absolute stereochemistry.



● HCl

L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN 5-Hexenoic acid, 2-[[[(1,1-dimethylethoxy)carbonyl]amino]-,  
 1,1-dimethylethyl ester, (2S)- (9CI)  
 MF C15 H27 N O4

Absolute stereochemistry.

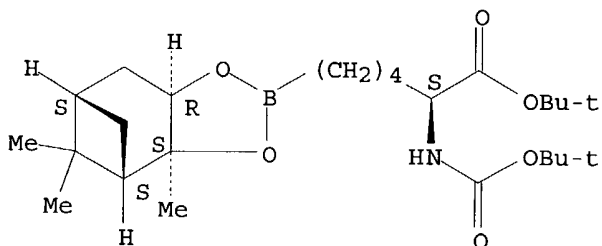


L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Borate (9CI)  
 MF Unspecified  
 CI COM, MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

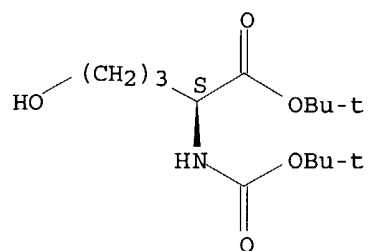
L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN 4,6-Methano-1,3,2-benzodioxaborole-2-hexanoic acid,  $\alpha$ -[[[(1,1-dimethylethoxy)carbonyl]amino]hexahydro-3a,5,5-trimethyl-,  
 1,1-dimethylethyl ester, ( $\alpha$ S,3aS,4S,6S,7aR)- (9CI)  
 MF C25 H44 B N O6

Absolute stereochemistry.



L2 8 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Norvaline, N-[[[(1,1-dimethylethoxy)carbonyl]-5-hydroxy-,  
 1,1-dimethylethyl ester (9CI)  
 MF C14 H27 N O5

Absolute stereochemistry.



ALL ANSWERS HAVE BEEN SCANNED

=> s norleucine and l2

L3                    5538 NORLEUCINE  
                      1 NORLEUCINE AND L2



=> s assay and arginase inhibitor antagonist

215913 ASSAY  
90055 ASSAYS  
280098 ASSAY  
    (ARGINASE OR ASSAYS)  
2722 ARGINASE  
113 ARGINASES  
2723 ARGINASE  
    (ARGINASE OR ARGINASES)  
323535 INHIBITOR  
346141 INHIBITORS  
528717 INHIBITOR  
    (INHIBITOR OR INHIBITORS)  
108645 ANTAGONIST  
75126 ANTAGONISTS  
142659 ANTAGONIST  
    (ANTAGONIST OR ANTAGONISTS)  
0 ARGINASE INHIBITOR ANTAGONIST  
    (ARGINASE(W) INHIBITOR(W) ANTAGONIST)  
L1 0 ASSAY AND ARGINASE INHIBITOR ANTAGONIST

=> s assay and arginase inhibitor

215913 ASSAY  
90055 ASSAYS  
280098 ASSAY  
    (ARGINASE OR ASSAYS)  
2722 ARGINASE  
113 ARGINASES  
2723 ARGINASE  
    (ARGINASE OR ARGINASES)  
323535 INHIBITOR  
346141 INHIBITORS  
528717 INHIBITOR  
    (INHIBITOR OR INHIBITORS)  
39 ARGINASE INHIBITOR  
    (ARGINASE(W) INHIBITOR)  
L2 3 ASSAY AND ARGINASE INHIBITOR

=> d ibib abs hitstr 1-3

L2 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:500684 CAPLUS

DOCUMENT NUMBER: 132:62184

TITLE: Functional and molecular characterization of nitric oxide synthase in the endometrium and myometrium of pregnant sheep during the last third of gestation

AUTHOR(S): Massmann, G. Angela; Zhang, Jie; Figueroa, Jorge P.

CORPORATE SOURCE: Perinatal Research Laboratory, Departments of Obstetrics and Gynecology, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA

SOURCE: Am. J. Obstet. Gynecol. (1999), 181(1), 116-125

CODEN: AJOGAH; ISSN: 0002-9378

PUBLISHER: Mosby, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study was undertaken to characterize the biochem. and expression profiles of the nitric oxide synthase isoforms present in the sheep uterus during late gestation. Myometrium and endometrium were obtained from 28 time-mated pregnant sheep that were under halothane general anesthesia. Tissues were kept frozen at -80°C until they were homogenized for the measurement of (1) nitric oxide synthase activity according to the

carbon 14-labeled arginine-citrulline conversion **assay**, (2) nitric oxide synthase protein mass according to Western blot anal., and (3) nitric oxide synthase mRNA according to the RNase protection **assay**. The nitric oxide synthase activity **assay** included 8 parallel treatments for biochem. characterization, in particular with the **arginase inhibitors** ornithine and (+)-S-2-amino-5-iodoacetamidopentanoic acid. The biochem. characterization of nitric oxide synthase indicated that the predominant form of nitric oxide synthase in endometrium and myometrium (80%-90%) was calcium-calmodulin dependent. In endometrium 50% of reduced NAD-dependent arginine metabolism was accounted for by the presence of alternative arginine metabolic pathways. Expressions of type 1 and type 3 nitric oxide synthase were demonstrated in endometrium and myometrium by Western blot and RNase protection **assay**. Although no significant decrease in nitric oxide synthase activity or protein mass was observed, a significant decrease in myometrial type 1 nitric oxide synthase mRNA occurred in sheep not in labor at 140 days' gestation ( $P < 0.05$  by anal. of variance; term is  $144 \pm 5$  days). In the gravid sheep uterus the predominant nitric oxide synthase isoforms are type 1 in myometrium and type 3 in endometrium. Despite a decrease in type 1 nitric oxide synthase mRNA, enzymic activity and type 1 nitric oxide synthase protein mass do not decrease before parturition.

REFERENCE COUNT: 26

REFERENCE(S): (1) Balon, T; J Appl Physiol 1997, V82, P359 CAPLUS  
 (2) Bansal, R; J Clin Invest 1997, V99, P2502 CAPLUS  
 (3) Bradford, M; Anal Biochem 1976, V72, P248 CAPLUS  
 (4) Dong, Y; Biol Reprod 1998, V59, P933 CAPLUS  
 (5) Dong, Y; J Reprod Fertil 1996, V107, P249 CAPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:524033 CAPLUS

DOCUMENT NUMBER: 129:199627

TITLE: An improved **assay** for measurement of nitric oxide synthase activity in biological tissues

AUTHOR(S): Giraldez, Roberto R.; Zweier, Jay L.

CORPORATE SOURCE: Molecular and Cellular Biophysics Laboratories, Department of Medicine, Division of Cardiology, The Johns Hopkins Medical Institutions, Baltimore, MD, 21224, USA

SOURCE: Anal. Biochem. (1998), 261(1), 29-35

CODEN: ANBCA2; ISSN: 0003-2697

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB While the L-arginine conversion **assay** has been utilized to measure nitric oxide synthase (NOS) activity in isolated enzyme and pure cell prepns., this method often fails to provide accurate measurements in whole tissues. Biol. tissues contain variable amts. of unlabeled substrate and enzymes are present which can compete for substrate or independently form the product L-citrulline. NOS-independent conversion of radiolabeled L-arginine to L-citrulline occurs due to arginase- and ornithine transcarbamylase-mediated reactions and this limits the accuracy of this **assay** for measurement of NOS activity. In heart tissue, NOS-independent L-citrulline formation was observed which could not be blocked by the NOS inhibitor L-NAME but was blocked by the **arginase inhibitor** L-ornithine. To eliminate the effect of arginase-mediated L-citrulline formation, KCl-washed membrane particulate fractions were obtained by high-speed centrifugation. While arginase-mediated nonspecific activity was 85% concentrated in the cytosol, 93% of NOS activity was localized within the particulate fraction of the heart. The remaining arginase activity found in the crude pellet was mostly removed by a one-step KCl wash purification and when incubation periods of 8 min were utilized specific and accurate measurements of NOS activity

were obtained. NOS enzymic properties were defined for rat heart preps. with a Km of 2.9  $\mu$ M for L-arginine. All NOS activity detected was calcium-dependent suggesting it originated from the constitutive endothelial isoform. Thus, NOS-independent activity can be largely eliminated from the heart tissue by assaying KCl-washed membrane particulate fractions and this enables accurate quantitation of NOS activity. (c) 1998 Academic Press.

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1980:619227 CAPLUS

DOCUMENT NUMBER: 93:219227

TITLE: Mechanism of action of mouse macrophages as antitumor effector cells: role of arginase

AUTHOR(S): Farram, E.; Nelson, D. S.

CORPORATE SOURCE: Kolling Inst. Med. Res., R. North Shore Hosp. Sydney, St. Leonards, 2065, Australia

SOURCE: Cell. Immunol. (1980), 55(2), 283-93

CODEN: CLIMB8; ISSN: 0008-8749

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cytotoxic macrophages, enriched by centrifugation through Percoll gradients, were obtained from the peritoneal cavities of mice bearing a tumor or injected i.p. with proteose peptone. Damage to target tumor cells was detected in microcytotoxicity **assays** and by inhibition of uptake of tritiated thymidine. Supernatants from cultured macrophages were cytotoxic. Cytotoxicity was inhibited by arginine, by the **arginase inhibitors** uric acid and adenosine, and by cyclic AMP, hydrocortisone, chloroquin, cytochalasin B, and colchicine, but not by cycloheximide, puromycin, mitomycin C, or actinomycin D; it was enhanced by indomethacin. Macrophages which were cytotoxic in vitro were also capable of suppressing tumor growth in vivo. The role of arginase secretion by macrophages in mediating this tumor cytotoxicity is discussed.

=> s arginase inhibitor

2722 ARGINASE

113 ARGINASES

2723 ARGINASE

(ARGINASE OR ARGINASES)

323535 INHIBITOR

346141 INHIBITORS

528717 INHIBITOR

(INHIBITOR OR INHIBITORS)

L3 39 ARGINASE INHIBITOR

(ARGINASE(W) INHIBITOR)

=> s l3 and muscle

202673 MUSCLE

40144 MUSCLES

210444 MUSCLE

(MUSCLE OR MUSCLES)

L4 3 L3 AND MUSCLE

=> d ibib abs 1-3

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:547966 CAPLUS

DOCUMENT NUMBER: 131:295396

TITLE: Biochemical and functional profile of a newly developed potent and isozyme-selective

**arginase inhibitor**

AUTHOR(S): Baggio, Ricky; Emig, Frances A.; Christianson, David W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish  
CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA  
SOURCE: J. Pharmacol. Exp. Ther. (1999), 290(3), 1409-1416  
CODEN: JPETAB; ISSN: 0022-3565  
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB An increase in arginase activity has been associated with the pathophysiol. of a number of conditions, including an impairment in nonadrenergic and noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal smooth muscle. An **arginase inhibitor** may rectify this condition. We compared the effects of a newly designed **arginase inhibitor**, 2(S)-amino-6-borono-hexanoic acid (ABH), with the currently available N $\omega$ -hydroxy-L-arginine (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS) smooth-muscle relaxation and the arginase activity in the IAS and other tissues. Arginase caused an attenuation of the IAS smooth-muscle relaxations by NANC nerve stimulation that was restored by the **arginase inhibitors**. L-HO-Arg but not ABH caused dose-dependent and complete reversal of N $\omega$ -nitro-L-arginine-suppressed IAS relaxation that was similar to that seen with L-arginine. Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated relaxation of the IAS. In the IAS, ABH was found to be  $\approx$ 250 times more potent than L-HO-Arg in inhibiting the arginase activity. L-HO-Arg was found to be 10 to 18 times more potent in inhibiting the arginase activity in the liver than in nonhepatic tissues. We conclude that arginase plays a significant role in the regulation of nitric oxide synthase-mediated NANC relaxation in the IAS. The advent of new and selective **arginase inhibitors** may play a significant role in the discrimination of arginase isoenzymes and have important pathophysiol. and therapeutic implications in gastrointestinal motility disorders.

REFERENCE COUNT: 43

REFERENCE(S): (1) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS  
(2) Biancani, P; Gastroenterology 1985, V89, P867 CAPLUS  
(3) Boucher, J; Biochem Biophys Res Commun 1994, V203, P1614 CAPLUS  
(4) Buga, G; Am J Physiol 1996, V271, PH1988 CAPLUS  
(5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:271330 CAPLUS

DOCUMENT NUMBER: 130:282369

TITLE: Preparation of borono amino acids as **arginase inhibitors**

INVENTOR(S): Christianson, David W.; Baggio, Ricky; Elbaum, Daniel

PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA

SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

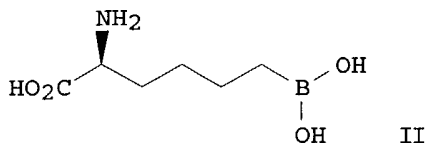
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919295	A1	19990422	WO 1998-US21430	19981009
W: AU, CA, JP, US				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
PT, SE

AU 9897979 A1 19990503 AU 1998-97979 19981009  
PRIORITY APPLN. INFO.: US 1997-61607 19971010  
WO 1998-US21430 19981009

OTHER SOURCE(S): MARPAT 130:282369  
GI



AB Title compds. HO<sub>2</sub>CCH(NH<sub>2</sub>)-Y<sub>1</sub>-Y<sub>2</sub>-Y<sub>3</sub>-Y<sub>4</sub>-B(OH)<sub>2</sub> (I; Y<sub>1</sub>-Y<sub>4</sub> = independently CH<sub>2</sub>, S, O, NH, N-alkyl; with the proviso that Y<sub>2</sub> ≠ S when Y<sub>1</sub> = Y<sub>3</sub> = Y<sub>4</sub> = CH<sub>2</sub>) are described. Compns. and methods for inhibiting arginase activity using I, including arginase activity in a mammal, are provided. Methods of making the compns. of the invention are also provided as are methods of using the compns. therapeutically. Thus, borono amino acid II, prepared in 5 steps from Boc-Glu-OCMe<sub>3</sub> via conversion to the side chain aldehyde, Wittig olefination with Ph<sub>3</sub>P:CH<sub>2</sub>, hydroboration with BH<sub>3</sub>, trapping with (1S,2S,4R,6S)-(+)-pinanediol, and deprotection with BCl<sub>3</sub>, inhibited arginase with K<sub>i</sub> = 0.1 μM.

REFERENCE COUNT: 2

REFERENCE(S): (1) Baggio, R; J Am Chem Soc 1997  
(2) Denniel, V; Tetrahedron Lett 1996

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:775272 CAPLUS

DOCUMENT NUMBER: 128:73284

TITLE: Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular smooth muscle cells. Role in polyamine biosynthesis

AUTHOR(S): Durante, William; Liao, Lan; Peyton, Kelly J.; Schafer, Andrew I.

CORPORATE SOURCE: Houston Veterans Administration Medical Center and the Department of Medicine, Baylor College of Medicine, Houston, TX, 77030, USA

SOURCE: J. Biol. Chem. (1997), 272(48), 30154-30159

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lysophosphatidylcholine (lyso-PC) is a major component of atherogenic lipids that stimulate vascular smooth muscle cell (SMC) proliferation. Because cationic amino acids are metabolized to growth-stimulatory polyamines, we examined whether lyso-PC regulates the transcellular transport and metabolism of cationic amino acids by vascular SMC. Treatment of SMC with lyso-PC initially (0-2 h) decreased cationic amino acid uptake, whereas longer exposures (6-24 h) progressively increased transport. Kinetic studies indicated that lyso-PC-induced inhibition was associated with a decrease in affinity for cationic amino acids, but the stimulation was mediated by an increase in transport capacity. Lyso-PC strongly induced the expression of cationic amino acid transporter-2 mRNA while modestly elevating the level of cationic amino acid transporter-1 mRNA. In addition, lyso-PC stimulated intracellular cationic amino acid metabolism by inducing ornithine decarboxylase activity and mRNA expression and also by inducing arginase activity in vascular

SMC. In contrast, lyso-PC inhibited the catabolism of L-arginine to nitric oxide by blocking inducible nitric oxide synthase expression. Lyso-PC increased markedly the capacity of SMC to generate putrescine, a polyamine, from extracellular L-ornithine and L-arginine. The lyso-PC-mediated increase in the production of putrescine was reversed by NG-methyl-L-arginine, a competitive inhibitor of cationic amino acid transport, or by  $\alpha$ -difluoromethylornithine, an ornithine decarboxylase inhibitor. The formation of putrescine from L-arginine was also prevented by **arginase inhibitor** NG-hydroxy-L-arginine. These results demonstrate that lyso-PC stimulates polyamine synthesis in vascular SMC by inducing the expression of the genes that regulate both the transport and metabolism of cationic amino acids. The actions of lyso-PC in stimulating cationic amino acid uptake and directing their metabolism to growth-stimulatory polyamines while simultaneously inhibiting the synthesis of antiproliferative NO, may contribute to lyso-PC-induced SMC proliferation and atherosclerotic lesion formation.

=> s assay

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          215913 ASSAY
          90055 ASSAYS
L5        280098 ASSAY
          (ASSAY OR ASSAYS)

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=> s l5 and muscle

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          202673 MUSCLE
          40144 MUSCLES
          210444 MUSCLE
          (MUSCLE OR MUSCLES)
L6        7011 L5 AND MUSCLE

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=> s arginase

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          2722 ARGINASE
          113 ARGINASES
L7        2723 ARGINASE
          (ARGINASE OR ARGINASES)

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=> s l6 and l7

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L8        2 L6 AND L7

```

=> d ibib abs 1-2

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:466757 CAPLUS

TITLE: Progression of hepatic stellate cell activation is associated with the level of oxidative stress rather than cytokines during CCl4-induced fibrogenesis

AUTHOR(S): Kim, Ki-Yong; Choi, Inpyo; Kim, Soung-Soo

CORPORATE SOURCE: Protein Laboratory, Mogam Biotechnology Research Institute, Kyonggi-Do, 449-910, S. Korea

SOURCE: Mol. Cells (2000), 10(3), 289-300

CODEN: MOCEEK; ISSN: 1016-8478

PUBLISHER: Springer-Verlag Singapore Pte. Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In order to identify a fibrogenic factor associated with the potential of hepatic stellate cells (HSC) activation that arises during the CCl4-induced fibrogenic process, the relationship between the activation

of HSC and levels of several fibrogenic factors were investigated. After isolation of HSC from the liver at different stages of CCl<sub>4</sub> intoxication, the activation of HSC was assessed by the expression of  $\alpha$ -smooth muscle actin. Levels of cytokines and oxidative stress in liver homogenates and plasma were measured by enzyme linked immunosorbent assay and the colorimetric method. In primary culture, HSC isolated from a rat liver were gradually activated in a time-dependent manner according to CCl<sub>4</sub> administration. The progression of HSC activation was closely correlated with parameters related to oxidative stress in liver homogenates rather than the tissue levels of several cytokines. Also, the levels of antioxidants and **arginase** activity were inversely correlated with HSC activation. In plasma, the levels of oxidative stress and cytokines in CCl<sub>4</sub>-treated rat livers were not associated with the activation of HSC found during the CCl<sub>4</sub>-induced fibrogenic process. The relationship between HSC activation and oxidative stress was also confirmed through several factor-treated HSC cultures. In conclusion, the activation of HSC was accelerated according to CCl<sub>4</sub> administration, and the progression of HSC activation is absolutely related to the oxidative stress. These results show that enhanced oxidative stress is an important signal for activation of HSC in exptl. liver fibrogenesis.

REFERENCE COUNT: 66

REFERENCE(S): (3) Barrett, E; Am J Physiol 1999, V276, PL979 CAPLUS  
(4) Beckman, J; Proc Natl Acad Sci USA 1990, V87, P1620 CAPLUS  
(5) Belyaev, N; Hepatology 1992, V15, P525 CAPLUS  
(6) Bonizzi, G; Biochem Pharmacol 2000, V59, P7 CAPLUS  
(7) Bredt, D; Proc Natl Acad Sci USA 1990, V87, P682 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:398234 CAPLUS

TITLE: Enzyme immunoassay for autoantibodies to human liver-type **arginase** and its clinical application

AUTHOR(S): Kimura, Masahiro; Tatsumi, Ke-Ita; Tada, Hisato; Ikemoto, Masaki; Fukuda, Yoshihiro; Kaneko, Akira; Kato, Michio; Hidaka, Yoh; Amino, Nobuyuki

CORPORATE SOURCE: Department of Laboratory Medicine, Osaka University Medical School, Osaka, 565-0871, Japan

SOURCE: Clin. Chem. (Washington, D. C.) (2000), 46(1), 112-117  
CODEN: CLCHAU; ISSN: 0009-9147

PUBLISHER: American Association for Clinical Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: **Arginase** is an enzyme of the urea cycle, and one of the two isoenzymes is the liver-type enzyme. We examined serum autoantibodies to this liver-type enzyme in patients with hepatitis. Methods: Antibodies to recombinant human liver-type **arginase** were measured by ELISA in 95 patients and 55 healthy controls. Results: The mean absorbance values in the ELISA **assays** of patients with definite autoimmune hepatitis (n = 11; P < 0.0001), probable autoimmune hepatitis (n = 31; P < 0.0001), and hepatitis C (HCV; n = 20; P < 0.01) were significantly different from those of healthy controls, but the values in patients with hepatitis B (HBV; n = 23) and other autoimmune diseases (n = 10) were not significantly different from those of healthy controls. When the cutoff was fixed at the upper 95th percentile of the absorbance value in healthy controls, pos. reactions were found in 18.2%, 32.3%, 20.0%, 13.0%, and 10.0% of patients with definite autoimmune hepatitis, probable autoimmune hepatitis, HCV hepatitis, HBV hepatitis, and other autoimmune diseases, resp. All of these pos. reactions were abolished by inhibition of serum with recombinant antigen. The specificity and sensitivity of this ELISA were 96% and 29%, resp. The intraassay and interassay coeffs.

of variation were 2.3-7.5% and 9.8-11%, resp. There was no relationship between these antibodies and anti-nuclear, anti-smooth **muscle**, or anti-cytochrome P450IID6 antibodies. Conclusions: The ELISA for anti-liver-type **arginase** autoantibody improved the detectability of autoimmune hepatitis when compared with established **assays** for liver-specific autoantibodies.

REFERENCE COUNT: 26

REFERENCE(S): (3) Dizikes, G; Biochem Biophys Res Commun 1986, V141, P53 CAPLUS  
 (4) Glass, R; J Biol Chem 1973, V248, P5785 CAPLUS  
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 (6) Gotoh, T; FEBS Lett 1996, V395, P119 CAPLUS  
 (7) Haraguchi, Y; Proc Natl Acad Sci 1987, V84, P412 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s arginase inhibitor

2722 ARGINASE  
 113 ARGINASES  
 2723 ARGINASE  
 (ARGINASE OR ARGINASES)  
 323535 INHIBITOR  
 346141 INHIBITORS  
 528717 INHIBITOR  
 (INHIBITOR OR INHIBITORS)

L9 39 ARGINASE INHIBITOR  
 (ARGINASE(W) INHIBITOR)

=> d ti 1-10

L9 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI L-arginine availability modulates local nitric oxide production and parasite killing in experimental trypanosomiasis

L9 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Characterization of nitric oxide synthase activity in the tropical sea anemone Aiptasia pallida

L9 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Effects of the New **Arginase Inhibitor**  
 Nω-Hydroxy-nor-L-Arginine on NO Synthase Activity in Murine Macrophages

L9 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Biochemical and functional profile of a newly developed potent and isozyme-selective **arginase inhibitor**

L9 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Functional and molecular characterization of nitric oxide synthase in the endometrium and myometrium of pregnant sheep during the last third of gestation

L9 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Preparation of borono amino acids as **arginase inhibitors**

L9 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI L-Arginine uptake and metabolism by lung macrophages and neutrophils following intratracheal instillation of silica in vivo

L9 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2000 ACS



TI An improved assay for measurement of nitric oxide synthase activity in biological tissues

L9 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Method and formulation of stimulating nitric oxide synthesis

L9 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI  $\alpha$ -Difluoromethylornithine (DFMO) as a potent arginase activity inhibitor in human colon carcinoma cells

=> d ti 11-39

L9 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Arginase modulates nitric oxide production in activated macrophages

L9 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Anti-MHV3 state induced by IFN gamma in macrophages is not related to arginine metabolism

L9 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Effects of L-valine on growth and polyamine metabolism in human colon carcinoma cells

L9 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular smooth muscle cells. Role in polyamine biosynthesis

L9 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Determination of nitric oxide synthase activity in rat, pig and rabbit prostate glands

L9 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Reduction of hair growth by **arginase inhibitors**

L9 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Nitric oxide synthase and arginase in cells isolated from the rat gastric mucosa

L9 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Preparation of arylamidinohydrazones for treatment of cachexia and nitric oxide-mediated diseases.

L9 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Antifertility effects of (+)-S-2-amino-6-iodoacetamidohexanoic acid (2-AIHA) in female rats

L9 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI N $\omega$ -hydroxyamino- $\alpha$ -amino acids as a new class of very strong inhibitors of arginases

L9 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Synthesis and effects on arginase and nitric oxide synthase of two novel analogs of N $\omega$ -hydroxyarginine, N $\omega$ -hydroxyindospicine and p-hydroxyamidinophenylalanine

L9 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI Inhibition of arginase by NG-hydroxy-L-arginine in alveolar macrophages: implications for the utilization of L-arginine for nitric oxide synthesis

L9 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2000 ACS

TI N $\omega$ -hydroxy-L-arginine, an intermediate in the L-arginine to nitric oxide pathway, is a strong inhibitor of liver and macrophage arginase

L9 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Antitumor effect and toxicity of two new active-site-directed irreversible ornithine decarboxylase and extrahepatic **arginase inhibitors**

L9 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Arginase as one of the inhibitory principles in the density-dependent as well as plasma membrane-mediated inhibition of liver cell growth in vivo

L9 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI The presence of an **arginase inhibitor** in the hemolymph of blowfly, *Aldrichina grahami*, after the larva stops eating

L9 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Mechanism of action of mouse macrophages as antitumor effector cells: role of arginase

L9 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Characteristics of arginases from plant, ureotelic, and uricotelic organisms

L9 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Arginase activity during the development of *Rana terrestris* tadpoles

L9 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Existence of hepatic **arginase inhibitors** in several tissues

L9 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI **Arginase inhibitor** from sunflower seeds: purification and inhibitory properties

L9 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Probable physiological role of an **arginase inhibitor** in uricotelic animal liver

L9 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Arginase inhibition of dialysable factor(s) from chick liver

L9 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Inhibitory factor(s) of arginase occurring in pigeon liver

L9 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Preliminary identification of the **arginase inhibitor** from sunflower seeds

L9 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Purification, properties, and inhibition of plant arginase

L9 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Microbiological and biochemical changes in sheep cheese

L9 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Relative depletion of an arginine-rich deoxyribonucleohistone component during tumor induction by the Shope papilloma virus

L9 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2000 ACS  
 TI Inhibitory factor(s) of rat liver arginase occurring in chick liver

=> s 19 and muscle

202673 MUSCLE

40144 MUSCLES  
210444 MUSCLE  
(MUSCLE OR MUSCLES)

L10 3 L9 AND MUSCLE

=> d ti 1-3

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS

TI Biochemical and functional profile of a newly developed potent and isozyme-selective **arginase inhibitor**

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS

TI Preparation of borono amino acids as **arginase inhibitors**

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2000 ACS

TI Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular smooth **muscle** cells. Role in polyamine biosynthesis

=> d ibib abs 1 3

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:547966 CAPLUS

DOCUMENT NUMBER: 131:295396

TITLE: Biochemical and functional profile of a newly developed potent and isozyme-selective **arginase inhibitor**

AUTHOR(S): Baggio, Ricky; Emig, Frances A.; Christianson, David W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish  
CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA

SOURCE: J. Pharmacol. Exp. Ther. (1999), 290(3), 1409-1416  
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An increase in arginase activity has been associated with the pathophysiol. of a number of conditions, including an impairment in nonadrenergic and noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal smooth **muscle**. An **arginase inhibitor** may rectify this condition. We compared the effects of a newly designed **arginase inhibitor**, 2(S)-amino-6-borohexanoic acid (ABH), with the currently available N $\omega$ -hydroxy-L-arginine (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS) smooth-**muscle** relaxation and the arginase activity in the IAS and other tissues. Arginase caused an attenuation of the IAS smooth-**muscle** relaxations by NANC nerve stimulation that was restored by the **arginase inhibitors**. L-HO-Arg but not ABH caused dose-dependent and complete reversal of N $\omega$ -nitro-L-arginine-suppressed IAS relaxation that was similar to that seen with L-arginine. Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated relaxation of the IAS. In the IAS, ABH was found to be  $\approx$ 250 times more potent than L-HO-Arg in inhibiting the arginase activity. L-HO-Arg was found to be 10 to 18 times more potent in inhibiting the arginase activity in the liver than in nonhepatic tissues. We conclude that arginase plays a significant role in the regulation of nitric oxide synthase-mediated NANC relaxation in the IAS. The advent of new and selective **arginase inhibitors** may play a significant role in the discrimination of arginase isoenzymes and have important pathophysiol. and therapeutic implications in gastrointestinal motility

disorders.

REFERENCE COUNT: 43  
REFERENCE(S): (1) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS  
(2) Biancani, P; Gastroenterology 1985, V89, P867 CAPLUS  
(3) Boucher, J; Biochem Biophys Res Commun 1994, V203, P1614 CAPLUS  
(4) Buga, G; Am J Physiol 1996, V271, PH1988 CAPLUS  
(5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:775272 CAPLUS

DOCUMENT NUMBER: 128:73284

TITLE: Lysophosphatidylcholine regulates cationic amino acid transport and metabolism in vascular smooth

**muscle** cells. Role in polyamine biosynthesis

AUTHOR(S): Durante, William; Liao, Lan; Peyton, Kelly J.; Schafer, Andrew I.

CORPORATE SOURCE: Houston Veterans Administration Medical Center and the Department of Medicine, Baylor College of Medicine, Houston, TX, 77030, USA

SOURCE: J. Biol. Chem. (1997), 272(48), 30154-30159  
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

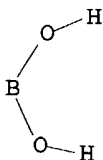
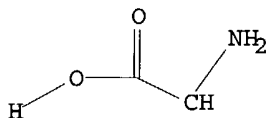
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lysophosphatidylcholine (lyso-PC) is a major component of atherogenic lipids that stimulate vascular smooth **muscle** cell (SMC) proliferation. Because cationic amino acids are metabolized to growth-stimulatory polyamines, we examined whether lyso-PC regulates the transcellular transport and metabolism of cationic amino acids by vascular SMC. Treatment of SMC with lyso-PC initially (0-2 h) decreased cationic amino acid uptake, whereas longer exposures (6-24 h) progressively increased transport. Kinetic studies indicated that lyso-PC-induced inhibition was associated with a decrease in affinity for cationic amino acids, but the stimulation was mediated by an increase in transport capacity. Lyso-PC strongly induced the expression of cationic amino acid transporter-2 mRNA while modestly elevating the level of cationic amino acid transporter-1 mRNA. In addition, lyso-PC stimulated intracellular cationic amino acid metabolism by inducing ornithine decarboxylase activity and mRNA expression and also by inducing arginase activity in vascular SMC. In contrast, lyso-PC inhibited the catabolism of L-arginine to nitric oxide by blocking inducible nitric oxide synthase expression. Lyso-PC increased markedly the capacity of SMC to generate putrescine, a polyamine, from extracellular L-ornithine and L-arginine. The lyso-PC-mediated increase in the production of putrescine was reversed by NG-methyl-L-arginine, a competitive inhibitor of cationic amino acid transport, or by  $\alpha$ -difluoromethylornithine, an ornithine decarboxylase inhibitor. The formation of putrescine from L-arginine was also prevented by **arginase inhibitor** NG-hydroxy-L-arginine. These results demonstrate that lyso-PC stimulates polyamine synthesis in vascular SMC by inducing the expression of the genes that regulate both the transport and metabolism of cationic amino acids. The actions of lyso-PC in stimulating cationic amino acid uptake and directing their metabolism to growth-stimulatory polyamines while simultaneously inhibiting the synthesis of antiproliferative NO, may contribute to lyso-PC-induced SMC proliferation and atherosclerotic lesion formation.

=> d

L1 HAS NO ANSWERS  
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

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SAMPLE SCREEN SEARCH COMPLETED - 23 TO ITERATE

100.0% PROCESSED 23 ITERATIONS  
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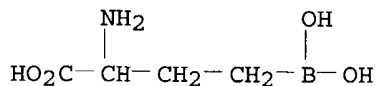
4 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
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L2 4 SEA SSS SAM L1

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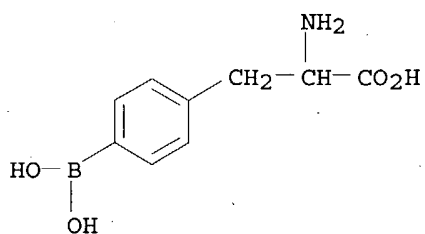
L2 4 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Butanoic acid, 2-amino-4-borono- (9CI)  
MF C4 H10 B N O4  
CI COM



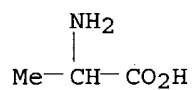
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L2 4 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Phenylalanine, 4-borono-, polymer with alanine (9CI)  
MF (C9 H12 B N O4 . C3 H7 N O2)x  
CI PMS

CM 1

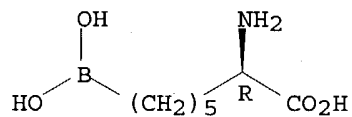


CM 2



L2 4 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Heptanoic acid, 2-amino-7-borono-, (R)- (9CI)  
 MF C7 H16 B N O4

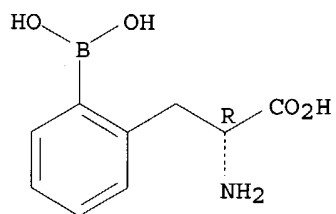
Absolute stereochemistry.



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L2 4 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN D-Phenylalanine, 2-borono- (9CI)  
 MF C9 H12 B N O4

Absolute stereochemistry.



ALL ANSWERS HAVE BEEN SCANNED

=> s l1 full

FULL SEARCH INITIATED 10:17:12 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 408 TO ITERATE

100.0% PROCESSED 408 ITERATIONS  
SEARCH TIME: 00.00.01

56 ANSWERS

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13701012 1-10/NR  
L4 37 L3 AND 1-10/NR

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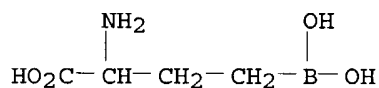
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=> s l3 not l4

L5 19 L3 NOT L4

=> d scan

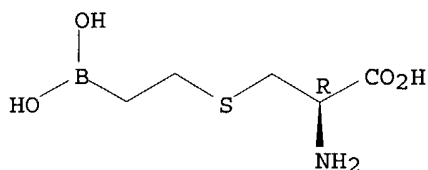
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Butanoic acid, 2-amino-4-borono- (9CI)  
MF C4 H10 B N O4  
CI COM



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI)  
MF C5 H12 B N O4 S . Cl H

Absolute stereochemistry.



● HCl

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS

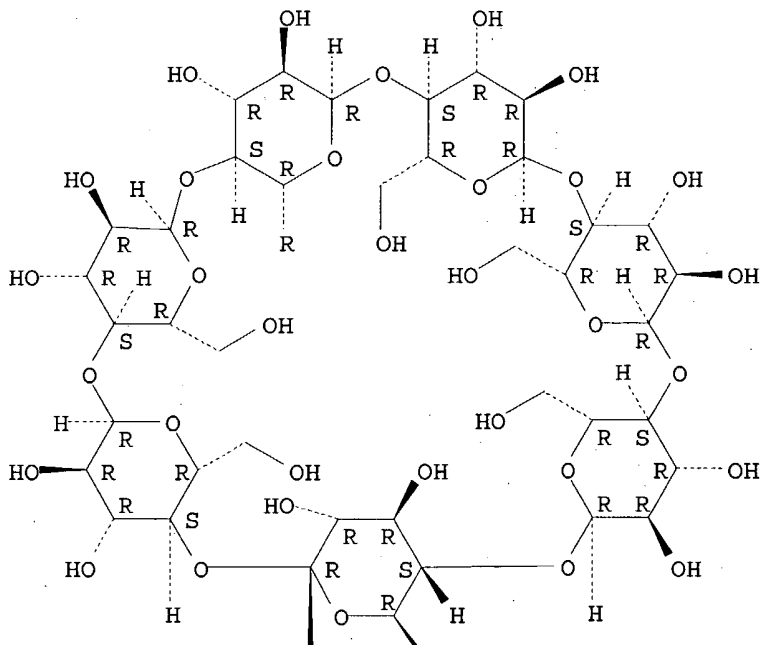
IN L-Phenylalanine, 4-borono-, compd. with O- $\alpha$ -D-glucopyranosyl-  
(1 $\rightarrow$ 4)-O- $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 6A)- $\beta$ -cyclodextrin  
(1:2) (9CI)

MF C54 H90 O45 . 1/2 C9 H12 B N O4

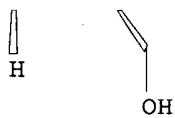
CM 1

Absolute stereochemistry.

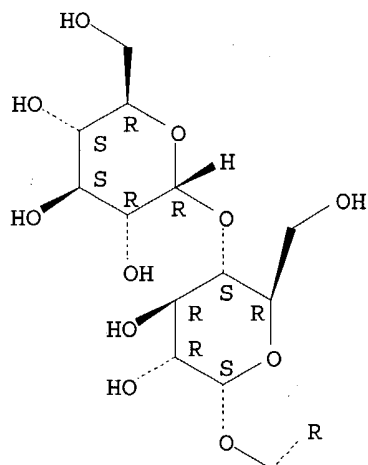
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PAGE 2-A

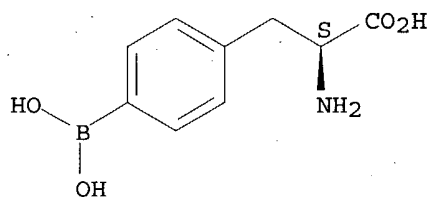






CM 2

Absolute stereochemistry. Rotation (-).

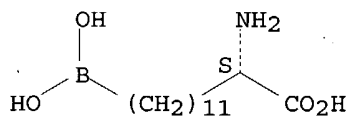


L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS

IN Tridecanoic acid, 2-amino-13-borono-, hydrochloride, (2S)- (9CI)

MF C13 H28 B N O4 . Cl H

Absolute stereochemistry.

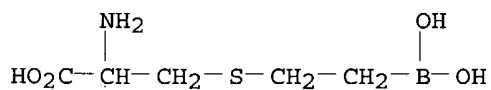


● HCl

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS

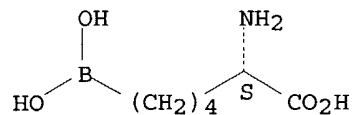
IN Alanine, 3-[(2-boronoethyl)thio]- (7CI)

MF C5 H12 B N O4 S



L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Norleucine, 6-borono-, hydrochloride (9CI)  
 MF C6 H14 B N O4 . Cl H

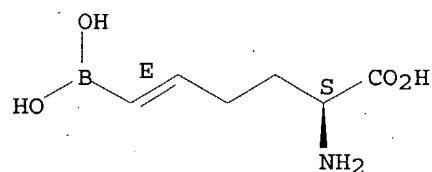
Absolute stereochemistry.



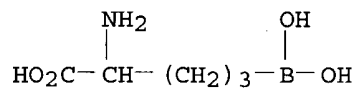
● HCl

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN 5-Hexenoic acid, 2-amino-6-borono-, (2S,5E)- (9CI)  
 MF C6 H12 B N O4

Absolute stereochemistry.  
 Double bond geometry as shown.



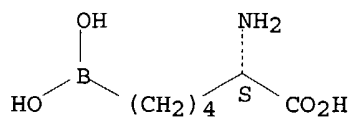
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Norvaline, 5-borono-, hydrochloride (9CI)  
 MF C5 H12 B N O4 . Cl H



● HCl

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Norleucine, 6-borono- (9CI)  
 MF C6 H14 B N O4  
 CI COM

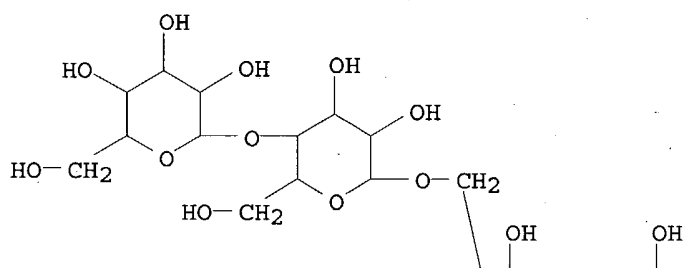
Absolute stereochemistry.

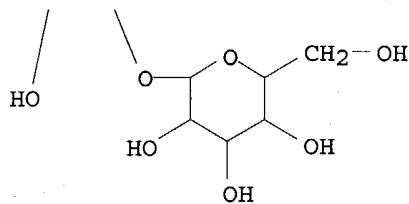
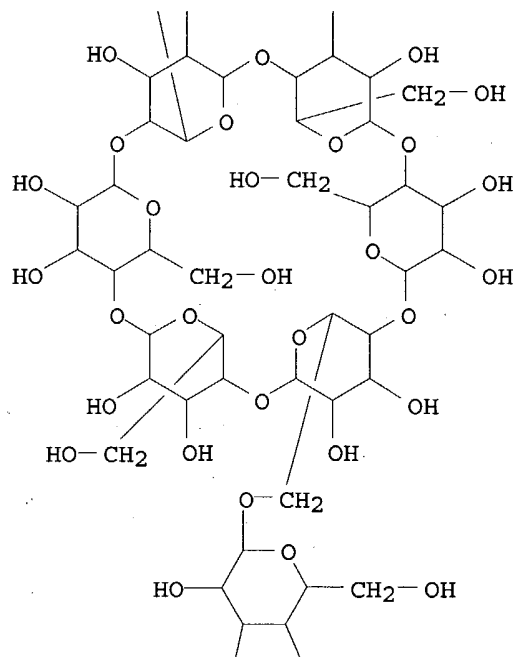


L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Phenylalanine, 4-borono-, compd. with O- $\alpha$ -D-glucopyranosyl-  
 (1 $\rightarrow$ 4)-O- $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 6A)-O-[O- $\alpha$ -D-  
 glucopyranosyl-(1 $\rightarrow$ 4)- $\alpha$ -D-glucopyranosyl-(1 $\rightarrow$ 6D)]-  
 $\alpha$ -cyclodextrin (1:2) (9CI)  
 MF C60 H100 O50 . 1/2 C9 H12 B N O4

CM 1

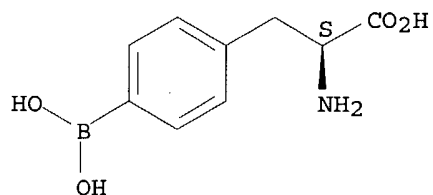
PAGE 1-A





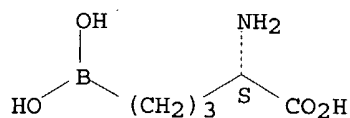
CM 2

Absolute stereochemistry. Rotation (-).



L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Norvaline, 5-borono-, hydrochloride (9CI)  
 MF C5 H12 B N O4 . Cl H

Absolute stereochemistry.

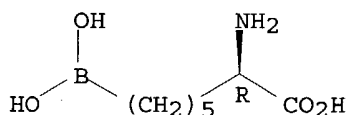


● HCl

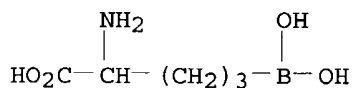
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Heptanoic acid, 2-amino-7-borono-, (R)- (9CI)  
MF C7 H16 B N O4

Absolute stereochemistry.

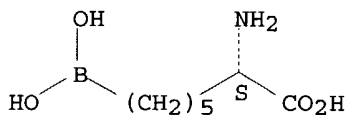


L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Norvaline, 5-borono- (9CI)  
MF C5 H12 B N O4  
CI COM

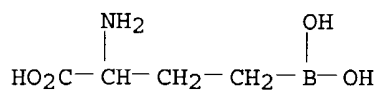


L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Heptanoic acid, 2-amino-7-borono-, (2S)- (9CI)  
MF C7 H16 B N O4

Absolute stereochemistry.



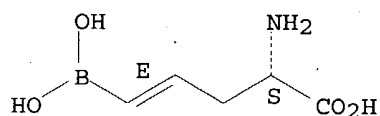
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Butanoic acid, 2-amino-4-borono-, hydrochloride (9CI)  
MF C4 H10 B N O4 . Cl H



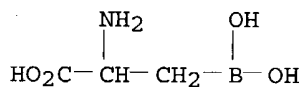
● HCl

L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN 4-Pentenoic acid, 2-amino-5-borono-, (2S,4E)- (9CI)  
 MF C5 H10 B N O4

Absolute stereochemistry.  
 Double bond geometry as shown.

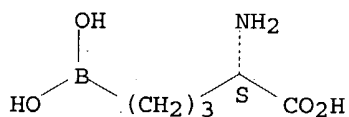


L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Alanine, 3-borono- (9CI)  
 MF C3 H8 B N O4



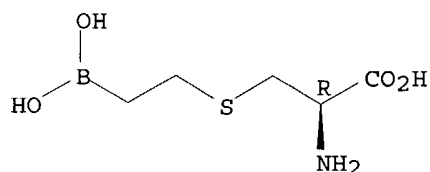
L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Norvaline, 5-borono- (9CI)  
 MF C5 H12 B N O4  
 CI COM

Absolute stereochemistry.



L5 19 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Cysteine, S-(2-boronoethyl)- (9CI)  
 MF C5 H12 B N O4 S  
 CI COM

Absolute stereochemistry.



ALL ANSWERS HAVE BEEN SCANNED

=> s 15 not Pentenoic

17453 PENTENOIC  
L6 18 L5 NOT PENTENOIC

=> s 16 not glucopyranosyl

101851 GLUCOPYRANOSYL  
L7 16 L6 NOT GLUCOPYRANOSYL

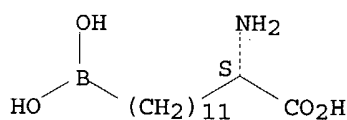
=> s 17 not Hexenoic

12923 HEXENOIC  
L8 15 L7 NOT HEXENOIC

=> d scan

L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Tridecanoic acid, 2-amino-13-borono-, hydrochloride, (2S)- (9CI)  
MF C13 H28 B N O4 . Cl H

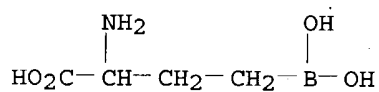
Absolute stereochemistry.



● HCl

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

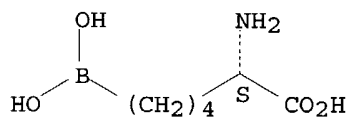
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Butanoic acid, 2-amino-4-borono-, hydrochloride (9CI)  
MF C4 H10 B N O4 . Cl H



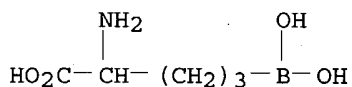
● HCl

L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Norleucine, 6-borono- (9CI)  
 MF C6 H14 B N O4  
 CI COM

Absolute stereochemistry.



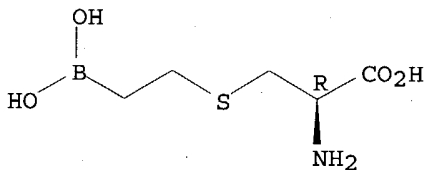
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Norvaline, 5-borono-, hydrochloride (9CI)  
 MF C5 H12 B N O4 . Cl H



● HCl

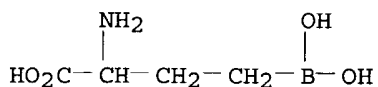
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI)  
 MF C5 H12 B N O4 S . Cl H

Absolute stereochemistry.



● HCl

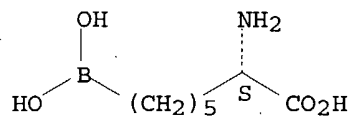
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Butanoic acid, 2-amino-4-borono- (9CI)  
 MF C4 H10 B N O4  
 CI COM



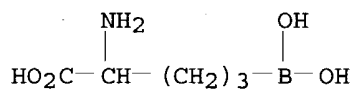


L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Heptanoic acid, 2-amino-7-borono-, (2S) - (9CI)  
 MF C7 H16 B N O4

Absolute stereochemistry.

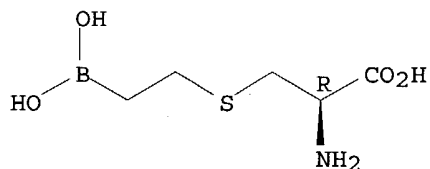


L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Norvaline, 5-borono- (9CI)  
 MF C5 H12 B N O4  
 CI COM



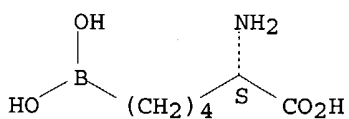
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Cysteine, S-(2-boronoethyl) - (9CI)  
 MF C5 H12 B N O4 S  
 CI COM

Absolute stereochemistry.



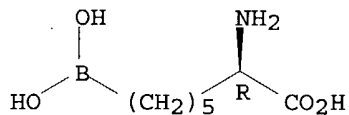
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN L-Norleucine, 6-borono-, hydrochloride (9CI)  
 MF C6 H14 B N O4 . Cl H

Absolute stereochemistry.



L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Heptanoic acid, 2-amino-7-borono-, (R)- (9CI)  
MF C7 H16 B N O4

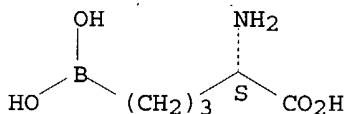
Absolute stereochemistry.



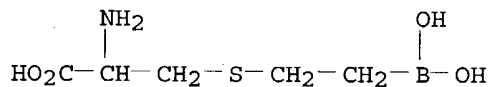
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN L-Norvaline, 5-borono- (9CI)  
MF C5 H12 B N O4  
CI COM

Absolute stereochemistry.

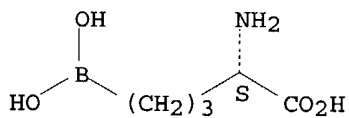


L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Alanine, 3-[(2-boronoethyl)thio]- (7CI)  
MF C5 H12 B N O4 S



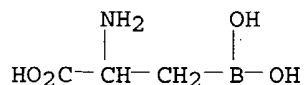
L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN L-Norvaline, 5-borono-, hydrochloride (9CI)  
MF C5 H12 B N O4 . Cl H

Absolute stereochemistry.



● HCl

L8 15 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
IN Alanine, 3-borono- (9CI)  
MF C3 H8 B N O4



ALL ANSWERS HAVE BEEN SCANNED

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FILE LAST UPDATED: 15 Aug 2000 (20000815/ED)

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=> s 18

L9 12 L8

=> d ibib abs hitstr 1-12

L9 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 2000:13532 CAPLUS  
DOCUMENT NUMBER: 132:322102  
TITLE: Synthesis and evaluation of ω-borono-α-amino acids as active-site probes of arginase and nitric oxide synthases  
AUTHOR(S): Collet, Sylvain; Carreaux, Francois; Boucher, Jean-Luc; Pethe, Stephanie; Lepoivre, Michel;

CORPORATE SOURCE: Danion-Bougot, Renee; Danion, Daniel  
 UMR 6510 CNRS, Synthèse et Electrosynthèse organiques,  
 Université Rennes I, Rennes, 35042, Fr.  
 SOURCE: Perkin 1 (2000), (2), 177-182  
 CODEN: PERKF9  
 PUBLISHER: Royal Society of Chemistry  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Enantiomerically pure  $\omega$ -borono- $\alpha$ -amino acids of various chain lengths have been synthesized according to a general methodol. involving condensation of alkenyl and alkynyl bromides with NiIII complex of the Schiff base derived from glycine and (S)-2-[N'-(N-benzylpropyl)amino]benzophenone, hydroboration of the intermediate  $\omega$ -unsatd.  $\alpha$ -amino acids with diisopinocampheylborane, oxidation with acetaldehyde. Some of these compds. act as potent inhibitors of rat liver and murine macrophage arginases, demonstrating that distance between the B(OH)<sub>2</sub> and  $\alpha$ -amino acid groups is a key determinant for their interaction with arginase. In contrast, they are without effect on neuronal and inducible NO synthases.

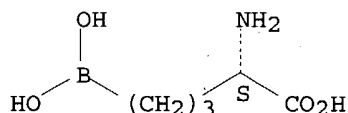
IT 212839-30-0  
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(synthesis and evaluation of enantiopure  $\omega$ -borono- $\alpha$ -amino acids as inhibitors of arginase and nitric oxide synthases)

RN 212839-30-0 CAPLUS

CN L-Norvaline, 5-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 222638-65-5P 266000-36-6P

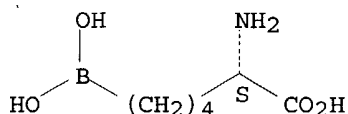
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and evaluation of enantiopure  $\omega$ -borono- $\alpha$ -amino acids as inhibitors of arginase and nitric oxide synthases)

RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

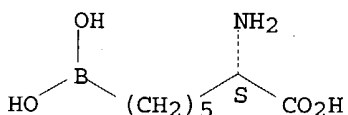
Absolute stereochemistry.



RN 266000-36-6 CAPLUS

CN Heptanoic acid, 2-amino-7-borono-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

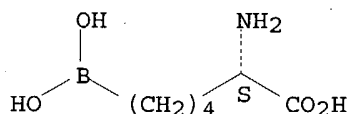


REFERENCE COUNT: 42  
 REFERENCE(S): (1) Aoyagi, Y; Phytochemistry 1985, V24, P1835 CAPLUS  
 (2) Babu, B; Curr Opin Chem Biol 1998, V2, P491 CAPLUS  
 (3) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS  
 (4) Bajgrowicz, J; Tetrahedron Lett 1984, V25, P2231 CAPLUS  
 (6) Belokon, Y; J Am Chem Soc 1985, V107, P4252 CAPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:799941 CAPLUS  
 DOCUMENT NUMBER: 132:148344  
 TITLE: A New Chromophoric Assay for Arginase Activity  
 AUTHOR(S): Baggio, Rick; Cox, J. David; Harper, Sandy L.;  
 Speicher, David W.; Christianson, David W.  
 CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of  
 Chemistry, University of Pennsylvania, Philadelphia,  
 PA, 19104-6323, USA  
 SOURCE: Anal. Biochem. (1999), 276(2), 251-253  
 CODEN: ANBCA2; ISSN: 0003-2697  
 PUBLISHER: Academic Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB It is reported that 1-nitro-3-guanidinobenzene (NGB) is a new assay  
 substrate for arginase, yielding products urea plus the chromophore  
 m-nitroaniline. The simple two-step synthesis of NGB is outlined. The  
 authors concluded with a description of its kinetic parameters and a brief  
 discussion of the utility of this assay. (c) 1999 Academic Press.  
 IT 222638-65-5  
 RL: BAC (Biological activity or effector, except adverse); BIOL  
 (Biological study)  
 (chromophoric assay for arginase activity using nitroguanidinobenzene  
 as substrate and study of enzyme inhibition by aminoboronohexanoic  
 acid)  
 RN 222638-65-5 CAPLUS  
 CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14  
 REFERENCE(S): (2) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS  
 (3) Bergeron, R; J Org Chem 1987, V52, P1700 CAPLUS  
 (4) Bewley, M; Structure 1999, V7, P435 CAPLUS  
 (5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS  
 (6) Christianson, D; Prog Biophys Mol Biol 1997, V67,  
 P217 CAPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:725889 CAPLUS  
 DOCUMENT NUMBER: 132:76677  
 TITLE: Arginase-boronic acid complex highlights a  
 physiological role in erectile function  
 AUTHOR(S): Cox, J. David; Kim, Noel N.; Traish, Abdulmaged M.;  
 Christianson, David W.  
 CORPORATE SOURCE: Roy and Diana Vagelos Laboratories, Department of

Chemistry, University of Pennsylvania, Philadelphia,  
PA, 19104-6323, USA

SOURCE: Nat. Struct. Biol. (1999), 6(11), 1043-1047  
CODEN: NSBIEW; ISSN: 1072-8368

PUBLISHER: Nature America

DOCUMENT TYPE: Journal

LANGUAGE: English

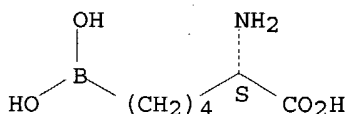
AB The crystal structure of the complex between the binuclear manganese metalloenzyme arginase and the boronic acid analog of L-arginine, 2(S)-amino-6-boronohexanoic acid (ABH), has been determined at 1.7 Å resolution from a crystal perfectly twinned by hemihedry. ABH binds as the tetrahedral boronate anion, with one hydroxyl oxygen sym. bridging the binuclear manganese cluster and a second hydroxyl oxygen coordinating to Mn2+A. This binding mode mimics the transition state of a metal-activated hydroxide mechanism. This transition state structure differs from that occurring in NO biosynthesis, thereby explaining why ABH does not inhibit NO synthase. We also show that arginase activity is present in the penis. Accordingly, the tight binding and specificity of ABH allows us to probe the physiol. role of arginase in modulating the NO-dependent smooth muscle relaxation required for erection. Strikingly, ABH causes significant enhancement of nonadrenergic, noncholinergic nerve-mediated relaxation of penile corpus cavernosum smooth muscle, suggesting that arginase inhibition sustains L-arginine concns. for NO synthase activity. Therefore, human penile arginase is a potential target for therapeutic intervention in the treatment of erectile dysfunction.

IT 222638-65-5D, arginase complexes  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(arginase-boronic acid complex highlights a physiol. role in erectile function)

RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35

REFERENCE(S): (1) Albina, J; J Immunol 1990, V144, P3877 CAPLUS  
(3) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS  
(4) Baggio, R; J Pharmacol Exp Ther 1999, V290, P1409 CAPLUS  
(5) Bewley, M; Structure 1999, V7, P435 CAPLUS  
(6) Brunger, A; Acta Crystallogr 1998, VD54, P905 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:547966 CAPLUS

DOCUMENT NUMBER: 131:295396

TITLE: Biochemical and functional profile of a newly developed potent and isozyme-selective arginase inhibitor

AUTHOR(S): Baggio, Ricky; Emig, Frances A.; Christianson, David W.; Ash, David E.; Chakder, Sushanta; Rattan, Satish

CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA

SOURCE: J. Pharmacol. Exp. Ther. (1999), 290(3), 1409-1416

PUBLISHER: CODEN: JPETAB; ISSN: 0022-3565  
American Society for Pharmacology and Experimental  
Therapeutics  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB An increase in arginase activity has been associated with the pathophysiol. of a number of conditions, including an impairment in nonadrenergic and noncholinergic (NANC) nerve-mediated relaxation of the gastrointestinal smooth muscle. An arginase inhibitor may rectify this condition. We compared the effects of a newly designed arginase inhibitor, 2(S)-amino-6-borono-hexanoic acid (ABH), with the currently available N $\omega$ -hydroxy-L-arginine (L-HO-Arg), on the NANC nerve-mediated internal anal sphincter (IAS) smooth-muscle relaxation and the arginase activity in the IAS and other tissues. Arginase caused an attenuation of the IAS smooth-muscle relaxations by NANC nerve stimulation that was restored by the arginase inhibitors. L-HO-Arg but not ABH caused dose-dependent and complete reversal of N $\omega$ -nitro-L-arginine-suppressed IAS relaxation that was similar to that seen with L-arginine. Both ABH and L-HO-Arg caused an augmentation of NANC nerve-mediated relaxation of the IAS. In the IAS, ABH was found to be  $\approx$ 250 times more potent than L-HO-Arg in inhibiting the arginase activity. L-HO-Arg was found to be 10 to 18 times more potent in inhibiting the arginase activity in the liver than in nonhepatic tissues. We conclude that arginase plays a significant role in the regulation of nitric oxide synthase-mediated NANC relaxation in the IAS. The advent of new and selective arginase inhibitors may play a significant role in the discrimination of arginase isoenzymes and have important pathophysiol. and therapeutic implications in gastrointestinal motility disorders.

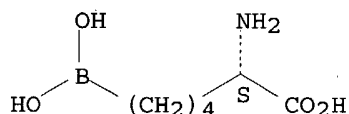
IT 222638-65-5

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (biochem. and functional profile of potent and isoenzyme-selective arginase inhibitor, 2(S)-amino-6-borono-hexanoic acid)

RN 222638-65-5 CAPLUS

CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43

REFERENCE(S): (1) Baggio, R; J Am Chem Soc 1997, V119, P8107 CAPLUS  
(2) Biancani, P; Gastroenterology 1985, V89, P867 CAPLUS  
(3) Boucher, J; Biochem Biophys Res Commun 1994, V203, P1614 CAPLUS  
(4) Buga, G; Am J Physiol 1996, V271, PH1988 CAPLUS  
(5) Cavalli, R; Biochemistry 1994, V33, P10652 CAPLUS  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:271330 CAPLUS

DOCUMENT NUMBER: 130:282369

TITLE: Preparation of borono amino acids as arginase inhibitors

INVENTOR(S): Christianson, David W.; Baggio, Ricky; Elbaum, Daniel

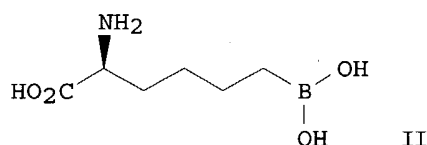
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA

SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919295	A1	19990422	WO 1998-US21430	19981009
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9897979	A1	19990503	AU 1998-97979	19981009
PRIORITY APPLN. INFO.:			US 1997-61607	19971010
			WO 1998-US21430	19981009
OTHER SOURCE(S):		MARPAT 130:282369		
GI				



AB Title compds. HO<sub>2</sub>CCH(NH<sub>2</sub>)-Y<sub>1</sub>-Y<sub>2</sub>-Y<sub>3</sub>-Y<sub>4</sub>-B(OH)<sub>2</sub> (I; Y<sub>1</sub>-Y<sub>4</sub> = independently CH<sub>2</sub>, S, O, NH, N-alkyl; with the proviso that Y<sub>2</sub> ≠ S when Y<sub>1</sub> = Y<sub>3</sub> = Y<sub>4</sub> = CH<sub>2</sub>) are described. Compns. and methods for inhibiting arginase activity using I, including arginase activity in a mammal, are provided. Methods of making the compns. of the invention are also provided as are methods of using the compns. therapeutically. Thus, borono amino acid II, prepared in 5 steps from Boc-Glu-OCMe<sub>3</sub> via conversion to the side chain aldehyde, Wittig olefination with Ph<sub>3</sub>P:CH<sub>2</sub>, hydroboration with BH<sub>3</sub>, trapping with (1S,2S,4R,6S)-(+) -pinanediol, and deprotection with BCl<sub>3</sub>, inhibited arginase with K<sub>i</sub> = 0.1 μM.

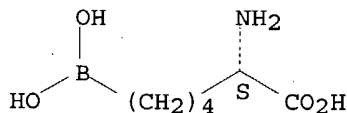
IT 194656-75-2P

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of borono amino acids as arginase inhibitors)

RN 194656-75-2 CAPLUS

CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

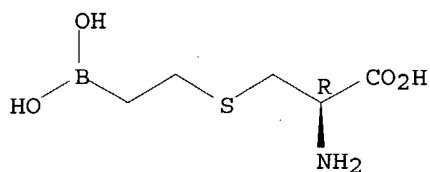
IT 63107-40-4P 212839-31-1P 222638-65-5P  
 222638-67-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of borono amino acids as arginase inhibitors)



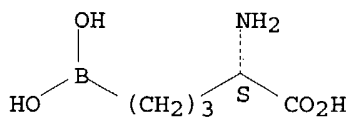
RN 63107-40-4 CAPLUS  
CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 212839-31-1 CAPLUS  
CN L-Norvaline, 5-borono-, hydrochloride (9CI) (CA INDEX NAME)

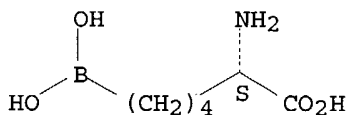
Absolute stereochemistry.



● HCl

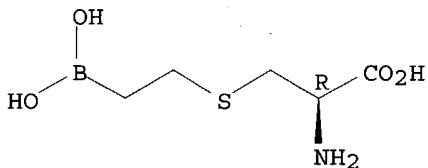
RN 222638-65-5 CAPLUS  
CN L-Norleucine, 6-borono- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 222638-67-7 CAPLUS  
CN L-Cysteine, S-(2-boronoethyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT:  
REFERENCE(S):

- 2  
(1) Baggio, R; J Am Chem Soc 1997  
(2) Denniel, V; Tetrahedron Lett 1996

L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:482481 CAPLUS

DOCUMENT NUMBER: 129:230968

TITLE: Stereoselective, nonracemic synthesis of  
 $\omega$ -borono- $\alpha$ -amino acids

AUTHOR(S): Collet, Sylvain; Bauchat, Patrick; Danion-Bougot,  
Renee; Danion, Daniel

CORPORATE SOURCE: Synthese et Electrosynthese Organiques, UMR 6510,  
Universite de Rennes I, Rennes, 35042, Fr.

SOURCE: Tetrahedron: Asymmetry (1998), 9(12), 2121-2131  
CODEN: TASYE3; ISSN: 0957-4166

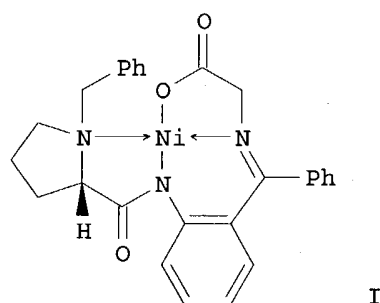
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 129:230968

GI



AB  $\omega$ -Unsatd.  $\alpha$ -amino acids are synthesized through condensation of allyl and propargyl bromides or of 9-bromoundecene with glycinate Schiff base Ni(II) complex I. Hydroboration with diisopinocampheylborane followed by oxidation with acetaldehyde affords enantiomerically pure  $\omega$ -borono- $\alpha$ -aminocarboxylic acids.

IT 212839-30-0P 212839-31-1P 212839-32-2P

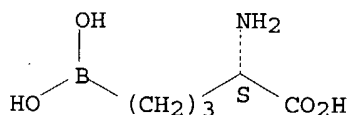
RL: SPN (Synthetic preparation); PREP (Preparation)

(stereoselective, nonracemic synthesis of borono amino acids via preparation and hydroboration of unsatd. amino acids)

RN 212839-30-0 CAPLUS

CN L-Norvaline, 5-borono- (9CI) (CA INDEX NAME)

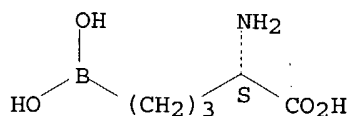
Absolute stereochemistry.



RN 212839-31-1 CAPLUS

CN L-Norvaline, 5-borono-, hydrochloride (9CI) (CA INDEX NAME)

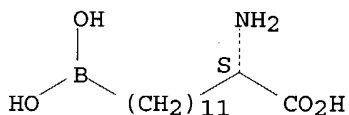
Absolute stereochemistry.



● HCl

RN 212839-32-2 CAPLUS  
CN Tridecanoic acid, 2-amino-13-borono-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L9 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:528761 CAPLUS

DOCUMENT NUMBER: 127:201930

TITLE: Inhibition of Mn<sup>2+</sup>-arginase by borate leads to the design of a transition state analog inhibitor, 2(S)-amino-6-boronohexanoic acid

AUTHOR(S): Baggio, Ricky; Elbaum, Daniel; Kanyo, Zoltan F.; Carroll, Patrick J.; Cavalli, R. Christopher; Ash, David E.; Christianson, David W.

CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104-6323, USA

SOURCE: J. Am. Chem. Soc. (1997), 119(34), 8107-8108

CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The tetrahedral borate anion is a modest inhibitor of Mn<sup>2+</sup>-arginase, a critical metalloenzyme of mammalian nitrogen metabolism The crystal structure of

the arginase-ornithine-borate complex reveals the net displacement of the solvent mol. bridging the binuclear manganese cluster by a borate oxygen atom in the native enzyme active site. Since this binding mode is reminiscent of the tetrahedral intermediate proposed for arginase-catalyzed arginine hydrolysis, it is postulated that a boronic acid-based arginine isostere would bind to arginase as the tetrahedral boronate anion and therefore mimic the tetrahedral intermediate and its flanking transition states in catalysis. Arginine isostere 2(S)-amino-6-boronohexanoic acid (I) was synthesized and evaluated for inhibition of arginase-catalyzed arginine hydrolysis. The results indicate that I is one of the most potent reversible inhibitors of arginase known to date with IC<sub>50</sub> = 0.8 μM. Complete kinetic characterization of I is complicated by nonlinearity of unknown origin (there is no evidence for slow-binding behavior), but competition binding expts. with N-hydroxyarginine indicate that K<sub>d</sub> ≤ 0.1 μM. Based on anal. of the crystal structure of the arginase-ornithine-borate

complex, a possible binding mode for I is postulated in which the metal-bridging solvent mol. observed in the native enzyme is displaced by an oxygen atom of the tetrahedral boronic acid anion.

IT 194656-75-2P

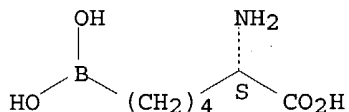
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(inhibition of  $Mn^{2+}$ -arginase by borate leads to the design of 2(S)-amino-6-boronohexanoic acid as a transition state analog inhibitor)

RN 194656-75-2 CAPLUS

CN L-Norleucine, 6-borono-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:454874 CAPLUS

DOCUMENT NUMBER: 125:222375

TITLE: Hydroboration of vinylglycine and allylglycine as a route to boron-derivatives of  $\alpha$ -amino acids

AUTHOR(S): Denniel, Valerie; Bauchat, Patrick; Danion, Daniel; Danion-Bougot, Renee

CORPORATE SOURCE: Groupe Rech. Physicochim. Struct., Univ. Rennes I, Rennes, 35042, Fr.

SOURCE: Tetrahedron Lett. (1996), 37(29), 5111-5114

CODEN: TELEAY; ISSN: 0040-4039

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 125:222375

AB The hydroboration of protected vinylglycine and allylglycine with dicyclohexyl- or diisopinocampheylborane occurs chemo- and regioselectively with attachment of boron to the less substituted end of the C:C double bond. Homoserine or  $\delta$ -hydroxynorvaline are readily obtained by H<sub>2</sub>O<sub>2</sub>/AcONa oxidation of dicyclohexylborane derivs. and 2-amino-4-boronobutanoic acid or 2-amino-5-boronopentanoic acid by reaction of diisopinocampheylborane derivs. with excess of acetaldehyde and deprotection.

IT 181312-07-2P 181312-08-3P 181312-09-4P

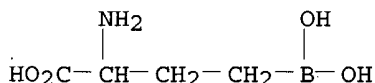
181312-10-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(hydroboration of vinylglycine and allylglycine in preparation of borono amino acids)

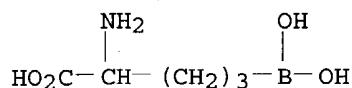
RN 181312-07-2 CAPLUS

CN Butanoic acid, 2-amino-4-borono-, hydrochloride (9CI) (CA INDEX NAME)



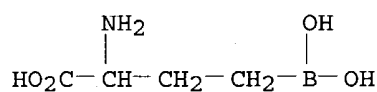
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RN 181312-08-3 CAPLUS  
CN Norvaline, 5-borono-, hydrochloride (9CI) (CA INDEX NAME)

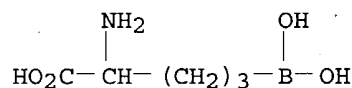


● HCl

RN 181312-09-4 CAPLUS  
CN Butanoic acid, 2-amino-4-borono- (9CI) (CA INDEX NAME)



RN 181312-10-7 CAPLUS  
CN Norvaline, 5-borono- (9CI) (CA INDEX NAME)



L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1990:77900 CAPLUS

DOCUMENT NUMBER: 112:77900

TITLE: Analogs of carbamyl aspartate as inhibitors of dihydroorotase: preparation of boronic acid transition-state analogs and a zinc chelator carbamylhomocysteine

AUTHOR(S): Kinder, David H.; Frank, Sandra K.; Ames, Matthew M.  
CORPORATE SOURCE: Dep. Oncol., Mayo Clin. Found., Rochester, MN, 55905, USA

SOURCE: J. Med. Chem. (1990), 33(2), 819-23  
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

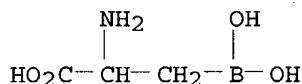
LANGUAGE: English

OTHER SOURCE(S): CASREACT 112:77900

AB Dihydroorotase (DHO) catalyzes the conversion of carbamylaspartate (CA) to dihydroorotate (DO) in the de novo pyrimidine biosynthetic pathway. Utilizing 2 mechanism-based strategies, we have designed and prepared potential DHO inhibitor analogs of CA. One strategy replaced the side-chain carboxyl moiety of CA with a boronic acid. This substitution yields compds. which form stable charged tetrahedral intermediates and mimic the enzyme-substrate transition state. Preparation of the boronic acid analogs of CA and its carboxylic acid esters focused on a Curtius rearrangement as a key step following a malonic ester synthesis. This was followed by carbamoylation of the free amine under nonaq. neutral conditions with Si(NCO)<sub>4</sub>. The Et ester was a competitive inhibitor of DHO with an apparent K<sub>i</sub> of 5.07 μM, while the nonesterified analog and the Me ester were not effective inhibitors. None of the compds. were

cytotoxic against L1210 cells in culture. An active-site-directed  
sulfhydryl-containing zinc chelator was also prepared This analog irreversibly  
inhibited the enzyme, but it also was ineffective in L1210 growth  
inhibition.

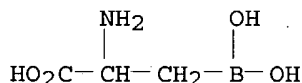
IT 108082-89-9  
RL: RCT (Reactant)  
(carbon-14-labeled carbamoylation of)  
RN 108082-89-9 CAPLUS  
CN Alanine, 3-borono- (9CI) (CA INDEX NAME)



L9 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1987:407557 CAPLUS  
DOCUMENT NUMBER: 107:7557  
TITLE: Synthesis of 2-amino-3-boronopropionic acid: a  
boron-containing analog of aspartic acid  
AUTHOR(S): Kinder, David H.; Ames, Matthew M.  
CORPORATE SOURCE: Dep. Oncol., Mayo Clin. Found., Rochester, MN, 55905,  
USA  
SOURCE: J. Org. Chem. (1987), 52(12), 2452-4  
CODEN: JOCEAH; ISSN: 0022-3263  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 107:7557

AB The boron-containing analog of aspartic acid, 2-amino-3-boronopropionic acid,  
in which the side chain carboxyl group has been replaced by a boronic acid  
group, was prepared by two principal reactions: a malonic ester alkylation  
with (chloromethyl)boronic esters, and, after saponification of one Et ester of  
the adduct, a modified Curtius rearrangement to introduce the amino group.  
Unlike  $\alpha$ -amino boronic esters, the primary  $\beta$ -amino boronic  
acids and esters reported are stable and do not undergo elimination  
reactions.

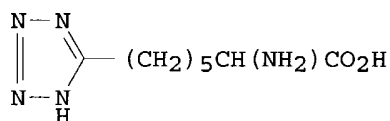
IT 108082-89-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)  
RN 108082-89-9 CAPLUS  
CN Alanine, 3-borono- (9CI) (CA INDEX NAME)



L9 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1983:198451 CAPLUS  
DOCUMENT NUMBER: 98:198451  
TITLE: Isomeric amino acids and their use in medicine  
PATENT ASSIGNEE(S): City of London Polytechnic, UK  
SOURCE: Belg., 23 pp.  
CODEN: BEXXAL  
DOCUMENT TYPE: Patent  
LANGUAGE: French  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 894116	A1	19830214	BE 1982-208817	19820813
SE 8204640	A	19830215	SE 1982-4640	19820810
NL 8203167	A	19830301	NL 1982-3167	19820812
FR 2511378	A1	19830218	FR 1982-14108	19820813
FR 2511378	B1	19860124		
GB 2104078	A	19830302	GB 1982-23363	19820813
GB 2104078	B2	19850123		
CH 656613	A	19860715	CH 1982-4869	19820813
JP 58131957	A2	19830806	JP 1982-141586	19820814
			GB 1981-24899	19810814

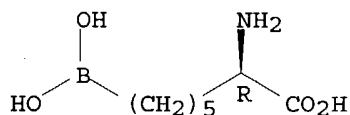
PRIORITY APPLN. INFO.:  
GI



AB (-)-D-Isomers of XQCH(NHR)CO<sub>2</sub>R<sub>1</sub> [Q = (un)substituted C<sub>5</sub> aliphatic radical; X = acid radical; R, R<sub>1</sub> = lipophilic radical, H, salts or pharmaceutically acceptable bioprecursors] were prepared by standard methods and exhibited anticonvulsant activity (no data). Thus, treating the Na salt of di-Et phosphite with 1,5-dibromopentane gave Br(CH<sub>2</sub>)<sub>5</sub>P(O)(OEt)<sub>2</sub>. Treating the latter with the Na salt of AcNHCH(CO<sub>2</sub>Et)<sub>2</sub>, followed by acid hydrolysis, gave (±)-H<sub>2</sub>O<sub>3</sub>P(CH<sub>2</sub>)<sub>5</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H. The latter was resolved by use of L-lysine. Also prepared were (-)-HO<sub>3</sub>S(CH<sub>2</sub>)<sub>5</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H, (-)-I, and (-)-(HO)<sub>2</sub>B(CH<sub>2</sub>)<sub>5</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H.

IT **85685-94-5P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and formation of lipophilic anticonvulsants from)  
 RN 85685-94-5 CAPLUS  
 CN Heptanoic acid, 2-amino-7-borono-, (R)- (9CI) (CA INDEX NAME)

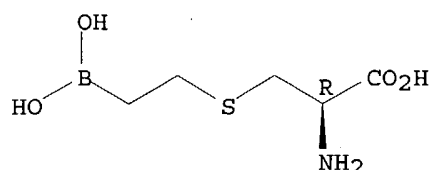
Absolute stereochemistry.



L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1977:406321 CAPLUS  
 DOCUMENT NUMBER: 87:6321  
 TITLE: Preparation and evaluation of immunoglobulins labeled with S-(2-boronoethyl)cysteine  
 AUTHOR(S): Hartz, Thomas Peter, Jr.  
 CORPORATE SOURCE: Memphis State Univ., Memphis, Tenn., USA  
 SOURCE: (1976) 87 pp. Avail.: Xerox Univ. Microfilms, Ann Arbor, Mich., Order No. 77-3150  
 From: Diss. Abstr. Int. B 1977, 37(8), 3927-8  
 DOCUMENT TYPE: Dissertation  
 LANGUAGE: English  
 AB Unavailable  
 IT **63107-40-4P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)

(labeling of immunoglobulins with, preparation and evaluation of)  
 RN 63107-40-4 CAPLUS  
 CN L-Cysteine, S-(2-boronoethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d it 12

L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2000 ACS  
 IT Immunoglobulins  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (labeled with (boronethyl)cysteines, preparation and evaluation of)  
 IT 63107-40-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (labeling of immunoglobulins with, preparation and evaluation of)

=> s l9 and arginase

2722 ARGINASE  
 113 ARGINASES  
 2723 ARGINASE  
 (ARGINASE OR ARGINASES)

L10 6 L9 AND ARGINASE

=> d ti 1-6

L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2000 ACS  
 TI Synthesis and evaluation of  $\omega$ -borono- $\alpha$ -amino acids as  
 active-site probes of **arginase** and nitric oxide synthases  
 L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2000 ACS  
 TI A New Chromophoric Assay for **Arginase** Activity  
 L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2000 ACS  
 TI **Arginase**-boronic acid complex highlights a physiological role in  
 erectile function  
 L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2000 ACS  
 TI Biochemical and functional profile of a newly developed potent and  
 isozyme-selective **arginase** inhibitor  
 L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2000 ACS  
 TI Preparation of borono amino acids as **arginase** inhibitors  
 L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2000 ACS  
 TI Inhibition of Mn<sup>2+</sup>-**arginase** by borate leads to the design of a  
 transition state analog inhibitor, 2(S)-amino-6-borohexanoic acid

=> file beilstein



COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY	SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
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FILE LAST UPDATED: 6 MAR 2000

FILE COVERS 1779 TO 2000.

\*\*\* CAS REGISTRY NUMBERS FOR 4,356,237 SUBSTANCES AVAILABLE \*\*\*

\*\*\* FILE CONTAINS 7,688,486 SUBSTANCES \*\*\*

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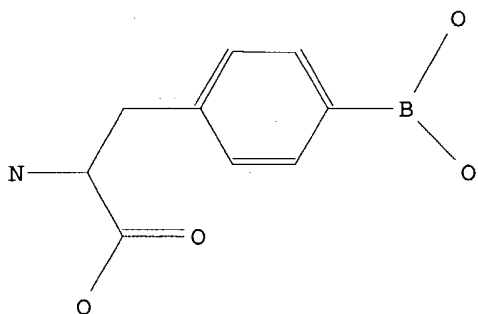
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L11 ANSWER 4 OF 4 COPYRIGHT 2000 BEILSTEIN CDS MDL

Beilstein Reg. No. (BRN): 3141428 Beilstein  
 Molecular Formula (MF): C9 H12 B N O4  
 Chemical Name (CN): 4-dihydroxyboranyl-phenylalanine  
 4-Dihydroxyboryl-phenylalanin  
 Beilstein Reference (SO): 4-16-00-01688  
 CAS Reg. No. (RN): 76410-58-7; 77374-29-9; 90580-64-6; 111821-49-9  
 Rltd. Stereoisomers (RSI): 4458616  
 Formula Weight (FW): 209.01  
 Lawson Number (LN): 16761



=> d ide 3

L11 ANSWER 3 OF 4 COPYRIGHT 2000 BEILSTEIN CDS MDL

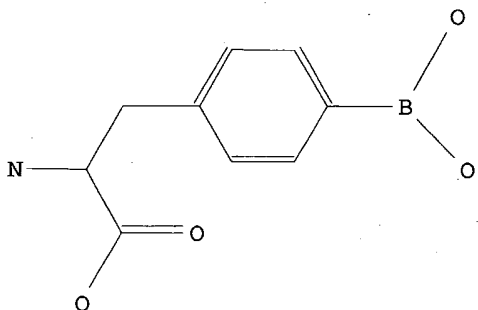
Beilstein Reg. No. (BRN): 3733224 Beilstein  
 Molecular Formula (MF): C<sub>9</sub> H<sub>12</sub> B N O<sub>4</sub> . (x) Cl H  
 Lin. Struct. Formula (LSF): C<sub>9</sub>H<sub>12</sub>BNO<sub>4</sub>\*(x)HCl  
 Chemical Name (CN): 4-dihydroxyboranyl-phenylalanine ; hydrochloride  
 4-Dihydroxyboryl-phenylalanin; Hydrochlorid  
 Beilstein Reference (SO): 4-16-00-01688  
 CAS Reg. No. (RN): 76410-59-8; 91196-68-8; 112725-17-4

Component Data:

Component Reg. No. (CBRN)	Component Molec. Formula (CMF)	Formula Weight (FW)	Lawson Number (LN)
3141428	C <sub>9</sub> H <sub>12</sub> B N O <sub>4</sub>	209.01	16761
1098214	Cl H	36.46	

CM 1

CBRN 3141428  
 CMF C<sub>9</sub> H<sub>12</sub> B N O<sub>4</sub>



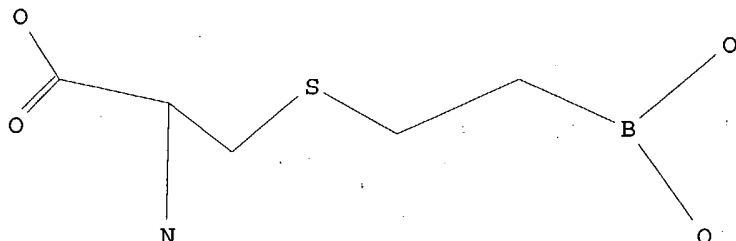
CM 2

CBRN 1098214  
CMF Cl H

=> d ide 2

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Beilstein Reg. No. (BRN): 4132291 Beilstein  
Molecular Formula (MF): C5 H12 B N O4 S  
Synonym (SY): S-<2-Borono-aethylthio>-cysteine  
Beilstein Reference (SO): 5-04  
CAS Reg. No. (RN): 63107-40-4; 88642-86-8  
Formula Weight (FW): 193.02  
Lawson Number (LN): 3813; 3544



=> d pre 2

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Preparation:

PRE

Start: BRN=1721406 cysteine, BRN=1768115 dibutoxy-vinyl-borane

Solv: methanol, H2O

Heating

Reference(s):

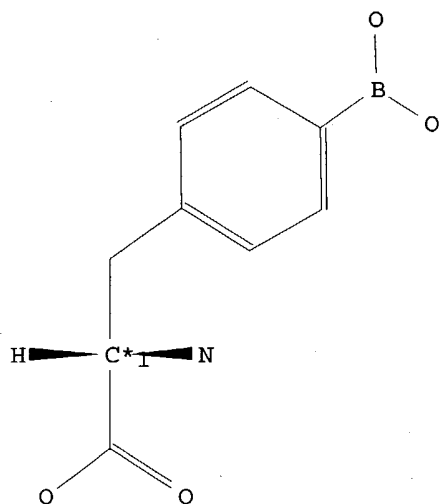
1. Matteson, D.S. et al., J. Med. Chem., 7 <1964>, 640-643, LA: EN, CODEN: JMCMAR

=> d ide 1

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Beilstein Reg. No. (BRN): 4458616 Beilstein  
Molecular Formula (MF): C9 H12 B N O4  
Synonym (SY): L-p-dihydroxyborylphenylalanine  
Beilstein Reference (SO): 6-16  
General Comments (NTE): Stereo compound  
CAS Reg. No. (RN): 76410-58-7; 77374-29-9; 90580-64-6; 111821-49-9

Rltd. Stereoisomers (RSI): 3141428  
Formula Weight (FW): 209.01  
Lawson Number (LN): 16761



Atom/Bond Notes:

1. CIP Descriptor: S

=> file caplus